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      Set  Items  Description
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? e au=waldmann


Ref   Items  Index-term
E1        3  AU=WALDMAN, S.
E2        7  AU=WALDMAN, W.
E3        0 *AU=WALDMANN
E4        1  AU=WALDMANN, D.
E5        1  AU=WALDMANN, E. R.
E6        8  AU=WALDMANN, H.
E7        1  AU=WALDMANN, M.
E8        4  AU=WALDMANN, R. A.
E9        1  AU=WALDMANN, T.
E10       3  AU=WALDMANN, T. A.
E11       2  AU=WALDMANN, U.
E12       1  AU=WALDMEIER, M.

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               3  AU=WALDMANN, T. A.
      S1       4  E9,E10
? t s1/3/all


 1/3/1
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1445930  NTIS Accession Number: PB89-200315
  Novel Interleukin 2 Receptor and Applications Thereof
  (Patent Applicatio)
  Waldmann, T. A. ; Leonard, W. J.
  Department of Health and Human Services, Washington, DC.
  Corp. Source Codes: 068119000
  Report No.: PAT-APPL-7-165 302
  Filed 8 Mar 88   18p
  Languages: English   Document Type: Patent
  Journal Announcement: GRAI8916
  See also PB87-218426.
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1351659  NTIS Accession Number: PB88-140231
  Method for Treating Maligancy and Autoimmune Disorders in Humans
  (Patent Applicatio)
  Waldmann, T. A.
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Department of Health and Human Services, Washington, DC.
Corp. Source Codes: 068119000
Report No.: PAT-APPL-7-085 707
Filed 17 Aug 87 18p
Languages: English Document Type: Patent
Journal Announcement: GRAI8808
This Government-owned invention available for U.S. licensing and, possibly, for foreign licensing. Copy of application available NTIS. Order this product from NTIS by: phone at 1-800-553-NTIS (U.S. customers); (703)605-6000 (other countries); fax at (703)321-8547; and email at orders@ntis.fedworld.gov. NTIS is located at 5285 Port Royal Road, Springfield, VA, 22161, USA.
NTIS Prices: PC A03/MF A01

1/3/3
DIALOG(R)File 6:NTIS

1325945 NTIS Accession Number: PB87-224424
Novel Interleukin 2 Receptor and Applications Thereof
(Patent Application)
Waldmann, T. A.
Department of Health and Human Services, Washington, DC.
Corp. Source Codes: 068119000
Report No.: PAT-APPL-7-066 989
Filed 29 Jun 87 16p
Languages: English Document Type: Patent
Journal Announcement: GRAI8723
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NTIS Prices: PC A02/MF A01

1/3/4
DIALOG(R)File 6:NTIS

1320089 NTIS Accession Number: PB87-218426
Novel Interleukin 2 Receptor and Applications Thereof
(Patent Application)
Waldmann, T.
Department of Health and Human Services, Washington, DC.
Corp. Source Codes: 068119000
Report No.: PAT-APPL-7-066 989
Filed 29 Jun 87 18p
Languages: English Document Type: Patent
Journal Announcement: GRAI8721
This Government-owned invention available for U.S. licensing and, possibly, for foreign licensing. Copy of application available NTIS.
NTIS Prices: Not available NTIS
? begin medtext

15mar00 08:06:04 User208760 Session D1481.3
$1.31 0.223 DialUnits File6
$7.20 4 Type(s) in Format 3
$7.20 4 Types
$8.51 Estimated cost File6
$0.10 TYMNET
$8.61 Estimated cost this search
$9.06 Estimated total session cost 0.423 DialUnits

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  File 442:AMA  Journals  1982-2000/Sep W1
        (c)2000 Amer Med Assn -FARS/DARS apply
  File 444:New England Journal of Med.  1985-2000/Feb W3
        (c) 2000 Mass. Med. Soc.
  File 457:The Lancet  1986-2000/Mar W1
        (c) 2000 The Lancet, Ltd.

      Set  Items  Description
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           5632  LYMPHOMA?
            194  TAC
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          31691  DOSE?
           2214  DOSING
          32314  MG
      S2     55  S1 AND (DOSE? OR DOSING OR MG)
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Cutaneous Graft-versus-Host Disease (ARTICLE)

  ARACTINGI, SELIM; CHOSIDOW, OLIVIER
  Archives of Dermatology
  May, 1998; Review: tzd602
  LINE COUNT: 00989


 2/3/2     (Item 2 from file: 442)
DIALOG(R)File 442:AMA  Journals
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00100896
COPYRIGHT American Medical Association 1996

Detection  of  Human  T-Cell  Lymphotrophic Virus Type I in Archival Tissue
Specimens (ARTICLE)

  WOOD,  GARY  S.;  RUFFO,  ALICE;  SALVEKAR,  ANUPAMA;  HENGHOLD,  WILL;
   TAKESHITA, MORISHIGE; KIKUCHI, MASAHIRO
  Archives of Dermatology
  Nov, 1996; Study: tzd1339
  LINE COUNT: 00413


 2/3/3     (Item 3 from file: 442)
DIALOG(R)File 442:AMA  Journals
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Circulating  Skin-Homing  T  Cells  in  Atopic  Dermatitis  Selective
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Up-regulation of HLA-DR, Interleukin-2R, and CD30 and Decrease After Combined UV-A and UV-B Phototherapy (ARTICLE)

PILETTA, PIERRE A.; WIRTH, SUSANNE; HOMMEL, LUCETTE; SAURAT, JEAN H.; HAUSER, CONRAD
Archives of Dermatology
Oct, 1996; Study: tzd1171
LINE COUNT: 00464

2/3/4 (Item 4 from file: 442)
DIALOG(R)File 442:AMA Journals

00094516

Peering at the Dermatology Literature (ARTICLE)

Archives of Dermatology
May, 1995; Editorials: de_602
LINE COUNT: 00366

2/3/5 (Item 5 from file: 442)
DIALOG(R)File 442:AMA Journals

00093606

Human T-Cell Lymphotropic Virus Type I-Associated Adult T-Cell **Leukemia** The Joseph Goldberger Clinical Investigator Lecture (ARTICLE)

WALDMANN, THOMAS A.
JAMA, The Journal of the American Medical Association
March 1, 1995; 9 of Health: tzj735
LINE COUNT: 00348

2/3/6 (Item 6 from file: 442)
DIALOG(R)File 442:AMA Journals

00090827

Recurrence of Pemphigus Vulgaris Associated With Interleukin 2 Therapy (ARTICLE)

PRUSSICK, RONALD; PLOTT, R. TODD; STANLEY, JOHN R.
Archives of Dermatology
July, 1994; Observation: de_890
LINE COUNT: 00266

2/3/7 (Item 7 from file: 442)
DIALOG(R)File 442:AMA Journals

00090215

Primary Gastric T-Cell **Lymphoma** Morphological and Immunohistochemical Studies of Two Cases (ARTICLE)

Archives of Pathology and Laboratory Medicine
May, 1994; Original Article: p547
LINE COUNT: 00257

2/3/8 (Item 8 from file: 442)
DIALOG(R)File 442:AMA Journals

00087400

(ARTICLE)
GOLDMAN, BARRY D.; OH, SE-KYUNG; DAVIS, BRET E.; KADIN, MARSHALL E.; POIESZ, BERNARD J.; KOH, HOWARD K.
Archives of Dermatology
Sep, 1993; OBSERVATION: p1166
LINE COUNT: 00294

2/3/9 (Item 9 from file: 442)
DIALOG(R)File 442:AMA Journals

00081309

Use and Interpretation of Diagnostic Immunologic Laboratory Tests (ARTICLE)

LOPEZ, MANUEL; FLEISHER, THOMAS; DESHAZO, RICHARD D.
JAMA, The Journal of the American Medical Association
November 25, 1992; 20: p2970
LINE COUNT: 01953

2/3/10 (Item 10 from file: 442)
DIALOG(R)File 442:AMA Journals

00055691

Administration of a Prostaglandin Synthetase Inhibitor Associated With an Increased Immune Cell Infiltrate in Squamous Cell Carcinoma of the Head and Neck (Article)

Shikani, Alan H. MD; Richtsmeier, William J. MD, Klein, Jerry L. PhD;Kopher, Kenneth A. MS
Archives of Otolaryngology-Head & Neck Surgery
1992; 118: 526 (3)

2/3/11 (Item 11 from file: 442)
DIALOG(R)File 442:AMA Journals

00055031

Interleukin 2 and Granulocyte-Macrophage Colony-Stimulating Factor Induce a Perivascular Lymphocytic Infiltrate in a Skin Explant Model (Article)

Horn, Thomas D., MD; Rest, Ellen B., MD; Karp, Judith E., MD; Burke, Philip J., MD; Vogelsang, Georgia B., MD; Boucher, Correne L.; Hood, Antoinette F., MD
Archives of General Psychiatry
1991; 48: 1789 (5)

2/3/12 (Item 12 from file: 442)
DIALOG(R)File 442:AMA Journals

00050927

Large-cell Anaplastic (Ki-1-Positive) **Lymphoma** Complicated by Disseminated Intravascular Coagulation (Article)

Arber, Daniel, MD; Bilbao, Jorge, MD; Bassion, Susan, PhD
Archives of Pathology & Laboratory Medicine
1991; 115: 188 (5)

2/3/13 (Item 13 from file: 442)
DIALOG(R)File 442:AMA Journals

00050311

Intravenous Administration of Recombinant Human Granulocyte-Macrophage Colony-Stimulating Factor Causes a Cutaneous Eruption (Article)

Horn, Thomas D., MD; Burke, Philip J., MD; Karp, Judith E., MD; Hood, Antoinette F., MD
Archives of Dermatology
1991; 127: 49 (4)

2/3/14 (Item 14 from file: 442)
DIALOG(R)File 442:AMA Journals

00049917

Human T-cell **Leukemia/Lymphoma** Viruses: Life Cycle, Pathogenicity, Epidemiology, and Diagnosis (Article)

Hjelle, Brian, MD
Archives of Pathology & Laboratory Medicine
1991; 115: 440 (11)

2/3/15 (Item 15 from file: 442)
DIALOG(R)File 442:AMA Journals

00046690

Childhood Ki-1 **Lymphoma**; A Report of Two Cases (ORIGINAL ARTICLES)

OKA, KUNIYUKI; MORI, NAOYOSHI; KOJIMA, MIZU; IIJIMA, TATSUO; HANADA, TAKASHI; TSUCHIDA, MASAHIRO
Archives of Pathology and Laboratory Medicine
September, 1989; 113: 998-1002
LINE COUNT: 00166 WORD COUNT: 02302

2/3/16 (Item 16 from file: 442)
DIALOG(R)File 442:AMA Journals

00040278

Cutaneous-Type Adult T-Cell **Leukemia/Lymphoma**; A Unique Clinical Feature With Monoclonal T-Cell Proliferation Detected by Southern Blot Analysis (OBSERVATIONS)

TAKAHASHI, KENZO; TANAKA, TOSHIHIRO; FUJITA, MAYUMI; HORIGUCHI, YUJI; MIYACHI, YOSHIKI; IMAMURA, SADAO
Archives of Dermatology
March, 1988; 124: 399-404
LINE COUNT: 00225 WORD COUNT: 03115

2/3/17 (Item 17 from file: 442)
DIALOG(R)File 442:AMA Journals

00038322

Human T-Cell Lymphotropic Virus Type I-Associated Adult T-Cell **Leukemia/Lymphoma** in an Atypical Host (ORIGINAL ARTICLE)

GOLDMAN-LEIKIN, ROBIN E.; HERST, C. V.; KIES, MERRILL S.; MARDER, ROBERT J.; ROSEN, STEVEN T.
Archives of Pathology and Laboratory Medicine
November, 1987; 111: 1054-1056
LINE COUNT: 00122 WORD COUNT: 01684

2/3/18 (Item 18 from file: 442)
DIALOG(R)File 442:AMA Journals

00037960

Coexisting Hodgkin's Disease and Mycosis Fungoides; Immunohistochemical Proof of Its Existence (ORIGINAL ARTICLE)

SIMRELL, CHARLES R.; BOCCIA, RALPH V.; JAFFE, ELAINE S.
Archives of Pathology and Laboratory Medicine
November, 1986; 110: 1029-1034
LINE COUNT: 00223 WORD COUNT: 03078

2/3/19 (Item 19 from file: 442)
DIALOG(R)File 442:AMA Journals

00029473

Nephrotic Syndrome Associated With a Clonal T-Cell **Leukemia** of Large Granular Lymphocytes With Cytotoxic Function (CLINICAL OBSERVATION)

ORMAN, STEPHEN V.; SCHECHTER, GERALDINE P.; WHANG-PENG, JACQUELINE; GUCCION, JOHN; CHAN, CLARA; SCHULOF, RICHARD S.; SHALHOUB, ROBERT J.
Archives of Internal Medicine
September, 1986; 146: 1827-1829
LINE COUNT: 00157 WORD COUNT: 02170

2/3/20 (Item 20 from file: 442)
DIALOG(R)File 442:AMA Journals

00025675

Sezary-like Syndrome in a 10-Year-Old Girl With Serologic Evidence of Human T-Cell Lymphotropic Virus Type I Infection (OBSERVATIONS)

IKAI, KOUICHI; UCHIYAMA, TAKASHI; MAEDA, MICHIYUKI; TAKIGAWA, MASAHIRO
Archives of Dermatology
October, 1987; 123: 1351-1355
LINE COUNT: 00149 WORD COUNT: 02069

2/3/21 (Item 21 from file: 442)

00025435

Actinic Reticuloid: An Immunohistochemical Study (CORRESPONDENCE; Vignettes)

TAKIGAWA, MASAHIRO
Archives of Dermatology
March, 1987; 123: 296-297
LINE COUNT: 00045 WORD COUNT: 00624

2/3/22 (Item 22 from file: 442)

00025414

New Therapies for Cutaneous T-Cell **Lymphoma** (EDITORIALS)

HEALD, PETER W.
Archives of Dermatology
February, 1987; 123: 189-191
LINE COUNT: 00122 WORD COUNT: 01697

2/3/23 (Item 23 from file: 442)

00025360

Lymphomatoid Papulosis; Histologic and Immunohistochemical Studies in a Patient With a Scaly Pigmented Eruption (STUDIES)

TOKURA, YOSHIKI; TAKIGAWA, MASAHIRO; OKU, TOMOZO; YAMADA, MIZUHO
Archives of Dermatology
December, 1986; 122: 1400-1405
LINE COUNT: 00215 WORD COUNT: 02972

2/3/24 (Item 24 from file: 442)

00017385

Positron Emission Tomography in Oncology; Council on Scientific Affairs; Report of the Positron Emission Tomography Panel (Topics in Radiology/Council Report)

JACOBSON, HAROLD G.
JAMA, The Journal of the American Medical Association
April 8, 1988; 259: 2126-2131
LINE COUNT: 00216 WORD COUNT: 02988

2/3/25 (Item 25 from file: 442)
DIALOG(R)File 442:AMA Journals

00016139

(FROM THE NIH)
WYNGAARDEN, BY JAMES B.
JAMA, The Journal of the American Medical Association
October 2, 1987; 258: 1707
LINE COUNT: 00076 WORD COUNT: 01052

2/3/26 (Item 26 from file: 442)
DIALOG(R)File 442:AMA Journals

00012709

Antitumor Strategies Based on Enhancing -- and Blocking -- Effects of Interleukin-2 (MEDICAL NEWS & PERSPECTIVES)

MERZ, BY BEVERLY
JAMA, The Journal of the American Medical Association
September 12, 1986; 256: 1241, 1244
LINE COUNT: 00114 WORD COUNT: 01577

2/3/27 (Item 1 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00120088

Prevention of Rejection in Cardiac Transplantation by Blockade of the Interleukin-2 Receptor with a Monoclonal Antibody (Original Articles)

Beniaminovitz, Ainat; Itescu, Silviu; Lietz, Katherine; Donovan, Mary; Burke, Elizabeth M.; Groff, Barbara D.; Edwards, Niloo; Mancini, Donna M.
The New England Journal of Medicine
Mar 2, 2000; 342 (9),pp 613-619
LINE COUNT: 00418 WORD COUNT: 05780

2/3/28 (Item 2 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00118604

Bone Marrow Involvement in Acute **Leukemia** (Images in Clinical Medicine)

Junghans, R.P.
The New England Journal of Medicine
Nov 5, 1998; 339 (19),p 1375
LINE COUNT: 00074 WORD COUNT: 01028

2/3/29 (Item 3 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00117715

Interleukin-2-Receptor Blockade with Daclizumab to Prevent Acute Rejection in Renal Transplantation (Original Articles)

Vincenti, Flavio; Kirkman, Robert; Light, Susan; Bumgardner, Ginny; Pescovitz, Mark; Halloran, Philip; Neylan, John; Wilkinson, Alan; Ekberg, Henrik; Gaston, Robert; Backman, Lars; Burdick, James; for the Daclizumab Triple Therapy Study Group.
The New England Journal of Medicine
Jan 15, 1998; 338 (3),pp 161-165
LINE COUNT: 00291 WORD COUNT: 04020

2/3/30 (Item 4 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00114651

Treatment of Adult T-Cell **Leukemia-Lymphoma** with a Combination of Interferon Alfa and Zidovudine (Original Articles)

Gill, Parkash S.; Harrington, William, Jr.; Kaplan, Mark H.; Ribeiro, Raul C.; Bennett, John M.; Liebman, Howard A.; Bernstein-Singer, Marjorie; Espina, Byron M.; Cabral, Lisa; Allen, Steven; Kornblau, Steven; Pike, Malcolm C.; Levine, Alexandra M.
The New England Journal of Medicine
Jun 29, 1995; 332 (26),pp 1744-1748
LINE COUNT: 00357 WORD COUNT: 04935

2/3/31 (Item 5 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00113528

Medical Progress: Renal Transplantation (Review Articles)

Suthanthiran, Manikkam; Strom, Terry B.
The New England Journal of Medicine
Aug 11, 1994; 331 (6),pp 365-376
LINE COUNT: 00629 WORD COUNT: 08682

2/3/32 (Item 6 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00113464

Current Concepts: Designer And Catalytic Antibodies (Review Article)

Mayforth, Ruth D.; Quintans, Jose.
The New England Journal of Medicine
Jul 19, 1990; 323 (3),pp 173-178
LINE COUNT: 00486 WORD COUNT: 06710

2/3/33 (Item 7 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00113334

Current Concepts: Designer And Catalytic Antibodies (Review Article)

Mayforth, Ruth D.; Quintans, Jose.
The New England Journal of Medicine
Jul 19, 1990; 323 (3),pp 173-178
LINE COUNT: 00486 WORD COUNT: 06710

2/3/34 (Item 8 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00112704

Seminars in Medicine of the Beth Israel Hospital, Boston: Cytokine Receptors In Congenital Hematopoietic Disease (Review Article)

D'Andrea, Alan D.
The New England Journal of Medicine
Mar 24, 1994; 330 (12),pp 839-846
LINE COUNT: 00579 WORD COUNT: 08002

2/3/35 (Item 9 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00111325

Seminars in Medicine of the Beth Israel Hospital, Boston: Pathogenesis Of Diseases Induced By Human Lymphotropic Virus Type I Infection (Review Articles)

Hollsberg, Per; Hafler, David A.
The New England Journal of Medicine
Apr 22, 1993; 328 (16),pp 1173-1182
LINE COUNT: 00561 WORD COUNT: 07742

2/3/36 (Item 10 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00109977

Hodgkin's Disease, **Lymphomatoid** Papulosis, And Cutaneous T-Cell **Lymphoma** Derived From A Common T-Cell Clone (Original Articles)

Davis, Thomas H.; Morton, Cynthia C.; Miller-Cassman, Robert; Balk, Steven P.; Kadin, Marshall E.
The New England Journal of Medicine
Apr 23, 1992; 326 (17),pp 1115-1122
LINE COUNT: 00421 WORD COUNT: 05813

2/3/37 (Item 11 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00108296

A Cluster Of Pneumocystis Carinii Pneumonia In Adults Without Predisposing Illnesses (Brief Report)

Jacobs, Jonathan L.; Libby, Daniel M.; Winters, Robert A.; Gelmont, David M.; Fried, Ethan D.; Hartman, Barry J.; Laurence, Jeffrey.
The New England Journal of Medicine
Jan 24, 1991; 324 (4),pp 246-250
LINE COUNT: 00467 WORD COUNT: 06445

2/3/38 (Item 12 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00107833

Current Concepts: Designer And Catalytic Antibodies (Review Article)

Mayforth, Ruth D.; Quintas, Jose.
The New England Journal of Medicine
Jul 19, 1990; 323 (3),pp 173-178
LINE COUNT: 00487 WORD COUNT: 06722

2/3/39 (Item 13 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00107419

Severe Combined Immunodeficiency Due To A Specific Defect In The Production Of Interleukin-2 (Brief Reports)

Weinberg, Kenneth; Parkman, Robertson.
The New England Journal of Medicine
Jun 14, 1990; 322 (24),pp 1718-1723
LINE COUNT: 00466 WORD COUNT: 06442

2/3/40 (Item 14 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00106381

Weekly Clinicopathological Exercises: Case 36-1989: A 34-Year-Old Jamaican Man With Fever, Hepatic Failure, Diarrhea, And A Progressive Gait Disorder (Case Records of the Massachusetts General Hospital)

Groopman, Jerome E.; Ferry, Judith A.
The New England Journal of Medicine
Sep 7, 1989; 321 (10),pp 663-675
LINE COUNT: 01042 WORD COUNT: 14379

2/3/41 (Item 15 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00106327

Pure Red-Cell Aplasia Of 10 Years' Duration Due To Persistent Parvovirus B19 Infection And Its Cure With Immunoglobulin Therapy (Medical Intelligence)

Kurtzman, Gary; Frickhofen, Norbert; Kimball, Janice; Jenkins, Douglas W.; Nienhuis, Arthur W.; Young, Neal S.
The New England Journal of Medicine
Aug 24, 1989; 321 (8),pp 519-523
LINE COUNT: 00393 WORD COUNT: 05426

2/3/42 (Item 16 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00104190

Pathogenic Human Retroviruses (Editorial)

Broder, Samuel
The New England Journal of Medicine
January 28, 1988; 318 (4),pp 243-245
LINE COUNT: 00301 WORD COUNT: 04164

2/3/43 (Item 17 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00102985

Remissions In Hairy-Cell **Leukemia** With Pentostatin (2'-Deoxycoformycin) (Original Article)

Spiers, Alexander S.D., T.D., Ph.D.; Moore, Dirk, Ph.D., Cassileth, Peter A., Harrington, David P., Ph.D., Cummings, Frank J.; Neiman, Richard S., Bennett, John M.; O'Connell, Michael J.
The New England Journal of Medicine
April 2, 1987; 316 (14),pp 825-830
LINE COUNT: 00439 WORD COUNT: 06069

2/3/44 (Item 18 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00102420

Concomitant Infection with HTLV-I and HTLV-III In A Patient with T8

Lymphoproliferative Disease (Medical Intelligence)

Harper, Mary E., Ph.D.; Kaplan, Mark H.; Marselle, Lisa M., B.A.; Pahwa, Savita G.; Chayt, Karen J.; Sarngadharan, M.G., Ph.D.; Wong-Staal,Flossie, Ph.D.; Gallo, Robert C.
The New England Journal of Medicine
October 23, 1986; 315 (17),pp 1073-1078
LINE COUNT: 00408 WORD COUNT: 05641

2/3/45 (Item 19 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00102091

A Second Isolate of HTLV-II Associated with Atypical Hairy-Cell **Leukemia** (Medical Intelligence)

Ronseblatt, Joseph D.; Golde, David W.; Wachsman, William, Ph.D.; Giorgi, Janis V., Ph.D.; Jacobs, Andrew; Schmidt, Gerhard M.; Quan, Shirley; Gasson, Judith C., Ph.D.; Chen, Irvin S.Y., Ph.D.
The New England Journal of Medicine
August 7, 1986; 315 (6),pp 372-377
LINE COUNT: 00564 WORD COUNT: 07793

2/3/46 (Item 20 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00101373

A Second Isolate of HTLV-II Associated with Atypical Hairy-Cell **Leukemia** (Medical Intelligence)

Ronseblatt, Joseph D.; Golde, David W.; Wachsman, William, Ph.D.; Giorgi, Janis V., Ph.D.; Jacobs, Andrew; Schmidt, Gerhard M.; Quan, Shirley; Gasson, Judith C., Ph.D.; Chen, Irvin S.Y., Ph.D.
The New England Journal of Medicine
August 7, 1986; 315 (6),pp 372-377
LINE COUNT: 00564 WORD COUNT: 07793

2/3/47 (Item 21 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00100709

T-Cell Receptor Gene Rearrangements as Clinical Markers of Human T-Cell **Lymphomas** (Original Article)

Bertness, Virginia, B.S.; Kirsch, Ilan; Hollis, Gregory, Ph.D.; Johnson, Bruce; Bunn, Paul A., Jr.
The New England Journal of Medicine
August 29, 1985; 313 (9),pp 534-538
LINE COUNT: 00579 WORD COUNT: 07994

2/3/48 (Item 22 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00100384

Subsets of Patients with Aplastic Anemia Identified by Flow Microfluorometry (Original Article)

Torok-Storb, Beverly, Ph.D.; Doney, Kristine; Sale, George; Thomas, E. Donnall; Storb, Rainer
The New England Journal of Medicine
April 18, 1985; 312 (16),pp 1015-1022
LINE COUNT: 00484 WORD COUNT: 06684

2/3/49 (Item 1 from file: 457)
DIALOG(R)File 457:The Lancet

00118363 (USE FORMAT 7 OR 9 FOR FULLTEXT)
TITLE: Human T-lymphotropic virus type I infection
Manns, Angela ; Hisada, Michie ; La Grenade, Lois
Viral Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, USA; Department of Medicine, University of the West Indies, Kingston, Jamaica
The Lancet, v353, n9168, pp 1951-1958
June 5, 1999

DOCUMENT TYPE: Journal; Seminar LANGUAGE: English RECORD TYPE: Fulltext
WORD COUNT: 5001

2/3/50 (Item 2 from file: 457)
DIALOG(R)File 457:The Lancet

00117541 (USE FORMAT 7 OR 9 FOR FULLTEXT)
TITLE: Immunosuppressive strategies in transplantation
Denton, Mark D ; Magee, Colm C ; Sayegh, Mohamed H
Laboratory of Immunogenetics and Transplantation, Renal Division, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, USA
The Lancet, v353, n9158, pp 1083-1091
March 27, 1999

DOCUMENT TYPE: Journal; Review LANGUAGE: English RECORD TYPE: Fulltext
WORD COUNT: 5609

2/3/51 (Item 3 from file: 457)
DIALOG(R)File 457:The Lancet

00104852 (USE FORMAT 7 OR 9 FOR FULLTEXT)
TITLE: Cutaneous T-cell **lymphoma** (mycosis fungoides)
Lorincz, Allan L
Section of Dermatology, University of Chicago, 5841 South Maryland, MC 5067, Chicago, IL 60637, USA
The Lancet, v347, n9005, pp 871-876
March 30, 1996

DOCUMENT TYPE: Journal; Skin cancer quartet LANGUAGE: English
RECORD TYPE: Fulltext
WORD COUNT: 3304

2/3/52 (Item 4 from file: 457)
DIALOG(R)File 457:The Lancet

00101288 (USE FORMAT 7 OR 9 FOR FULLTEXT)
TITLE: Impairment of leukaemia-free survival by addition of interleukin-2-receptor antibody to standard graft-versus-host prophylaxis
Blaise, Didier ; Olive, Daniel ; Michallet, Mauricette ; Marit, Gerald ; Leblond, Veronique ; Maraninchi, Dominique
Institut Paoli Calmettes and Inserm U119, Marseille; Hopital Edouard Herriot, Lyon; Hopital Haut Leveque, Bordeaux, Hopital Pitie-Salpetriere, Paris, France.
The Lancet, v345, n8958, pp 1144-1146
May 6, 1995

DOCUMENT TYPE: Journal; Articles LANGUAGE: English RECORD TYPE: Fulltext
WORD COUNT: 1856

2/3/53 (Item 5 from file: 457)
DIALOG(R)File 457:The Lancet

00088561 (USE FORMAT 7 OR 9 FOR FULLTEXT)
TITLE: Short Reports: Therapeutic effects of genetically engineered toxin (DAB sub 486 IL-2) in patient with chronic lymphocytic leukaemia
LeMaistre, Charles F|Rosenblum, Michael G|Reuben, James M|Parkinson, David R|Meneghetti, Carole M|Parker, Karen|Shaw, Jill P|Deisseroth, Albert B|Woodworth, Thasia
Department of Medicine/Hematology, University of Texas Health Science Center, San Antonio. Department of Hematology, Department of Clinical Immunology an Biological Therapy and Department of Laboratory Medicine, University of Texas MD Anderson Cancer Centre, Houston, Texas. National Cancer Institute, Bethesda, Maryland. Seragen, Inc., Hopkinton, Massachusetts, USA. Correspondence: Dr C. F. LeMaistre, University of Texas Health Science Center, Department of Medicine/Hematology, 7703 Floyd Curl Drive, San Antonio, Texas 78284-7880, USA.
The Lancet, v337, n8750, pp 1124-1125
1991 May 11

DOCUMENT TYPE: Journal; Report (REP) LANGUAGE: English RECORD TYPE: Fulltext
WORD COUNT: 993

2/3/54 (Item 6 from file: 457)
DIALOG(R)File 457:The Lancet

00082387 (USE FORMAT 7 OR 9 FOR FULLTEXT)
TITLE: Original Article: Effects of intradermal gamma-interferon in cutaneous leishmaniasis
Harms, G|Zwingenberger, K|Chehade, A K|Talhari, S|Racz, P|Mouakeh, A|Douba, M|Nakel, L|Naiff, R D|Kremsner, P G|Feldmeier, H|Bienzle, U
Landesinstitut fur Tropenmedizin, Berlin, Federal Republic of Germany. Departement de Dermato-Venereologie, Faculte de Medecine, Universite d'Alep, Syria. Centro de Dermatologia Tropical e Venereologia "Alfredo da Matta", Manaus, Brazil. Bernhard-Nocht-Institut fur Tropenmedizin, Abteilung fur Pathologie, Hamburg, Federal Republic of Germany. Instituto Nacional de Pesquisa da Amazonia, Departamento de Leishmaniose, Manaus, Brazil. Correspondence: G. H., Landesinstitut fur Tropenmedizin, Koenigin-Elisabeth-Strasse 32, 1 Berlin 19, FRG.
The Lancet, v333, n8650, pp 1287-1292
1989 Jun 10

DOCUMENT TYPE: Journal; Article (ART) LANGUAGE: English RECORD TYPE: Fulltext
WORD COUNT: 3343

2/3/55 (Item 7 from file: 457)
DIALOG(R)File 457:The Lancet

00075191 (USE FORMAT 7 OR 9 FOR FULLTEXT)
TITLE: Original Articles: Serum reactivity to human T-cell leukaemia/ **lymphoma** virus type I proteins in patients with large granular lymphocytic leukaemia
Starkebaum, Gordon|Loughran, Thomas P Jr|Kalyanaraman, V S|Kadin, Marshall E|Kidd, Pamela G|Singer, Jack W|Ruscetti, Francis W
Department of Medicine, Veterans Administration Medical Center, Seattle, Washington. Fred Hutchinson Cancer Research Center, Seattle. Centers for Disease Control, Atlanta, Georgia. Department of Pathology and Charles A. Dana Research Laboratory, Beth Israel Hospital and Harvard Medical School, Boston, Massachusetts. Department of Medicine and Laboratory Medicine, University of Washington, Seattle. National Cancer Institute, Frederick Cancer Research Facility, Frederick, Maryland, USA. Correspondence: G. S., Medical Service (111), VA Medical Center, 1660 S. Columbian Way, Seattle, Washington 98108, USA.
The Lancet, v329, n8533, pp 596-598
1987 Mar 14

DOCUMENT TYPE: Journal; Article (ART) LANGUAGE: English RECORD TYPE: Fulltext
WORD COUNT: 1984
? s s1 and py=1993

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            78  S1
          9725  PY=1993
     S3      2  S1 AND PY=1993
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? t s3/3/all

3/3/1 (Item 1 from file: 442)
DIALOG(R)File 442:AMA Journals

00087400

(ARTICLE)
GOLDMAN, BARRY D.; OH, SE-KYUNG; DAVIS, BRET E.; KADIN, MARSHALL E.; POIESZ, BERNARD J.; KOH, HOWARD K.
Archives of Dermatology
Sep, **1993**; OBSERVATION: p1166
LINE COUNT: 00294

3/3/2 (Item 1 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00111325

Seminars in Medicine of the Beth Israel Hospital, Boston: Pathogenesis Of Diseases Induced By Human Lymphotropic Virus Type I Infection (Review Articles)

Hollsberg, Per; Hafler, David A.
The New England Journal of Medicine
Apr 22, **1993**; 328 (16),pp 1173-1182

LINE COUNT: 00561 WORD COUNT: 07742

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? s s1 and py=1994

            78  S1
          9636  PY=1994
     S4      4  S1 AND PY=1994
? t s4/3/all
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4/3/1 (Item 1 from file: 442)
DIALOG(R)File 442:AMA Journals

00090827

Recurrence of Pemphigus Vulgaris Associated With Interleukin 2 Therapy (ARTICLE)

PRUSSICK, RONALD; PLOTT, R. TODD; STANLEY, JOHN R.
Archives of Dermatology
July, **1994**; Observation: de_890
LINE COUNT: 00266

4/3/2 (Item 2 from file: 442)
DIALOG(R)File 442:AMA Journals

00090215

Primary Gastric T-Cell **Lymphoma** Morphological and Immunohistochemical Studies of Two Cases (ARTICLE)

Archives of Pathology and Laboratory Medicine
May, **1994**; Original Article: p547
LINE COUNT: 00257

4/3/3 (Item 1 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00113528

Medical Progress: Renal Transplantation (Review Articles)

Suthanthiran, Manikkam; Strom, Terry B.
The New England Journal of Medicine
Aug 11, **1994**; 331 (6),pp 365-376
LINE COUNT: 00629 WORD COUNT: 08682

4/3/4 (Item 2 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00112704

Seminars in Medicine of the Beth Israel Hospital, Boston: Cytokine Receptors In Congenital Hematopoietic Disease (Review Article)

D'Andrea, Alan D.

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  The New England Journal of Medicine
  Mar 24, 1994; 330 (12),pp 839-846
  LINE COUNT: 00579          WORD COUNT: 08002
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  $138.11  Estimated cost this search
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File 159:Cancerlit  1975-2000/Mar
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             72  S2
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? s s2 and py=1994

             72  S2
          83740  PY=1994
      S4      4  S2 AND PY=1994
? t s3/3/all


 3/3/1
DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

01034122   94003208   MEDL/94003208
  The interleukin-2 receptor: a target for monoclonal antibody treatment of
human T-cell lymphotrophic virus I-induced adult T-cell leukemia.
  Waldmann TA; White JD; Goldman CK; Top L; Grant A; Bamford R;
Roessler E; Horak ID; Zaknoen S; Kasten-Sportes C; et al
  Metabolism Branch and Laboratory of Pathology, National Cancer Institute,
National Institutes of Health, Bethesda, MD 20892.
  Blood; 82(6):1701-12 1993  ISSN 0006-4971   Journal Code: A8G
  Languages: ENGLISH
  Document Type: JOURNAL ARTICLE


 3/3/2
DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

01029144   93368196   MEDL/93368196
  1992 Stohlman Memorial Lecture: targeting the IL-2 receptor.
  Waldmann TA
  Metabolism Branch, National Cancer Institute, National Institutes of
Health, Bethesda, MD 20892.
  Leukemia; 7 Suppl 2:S151-6 1993  ISSN 0887-6924   Journal Code: LEU
  Languages: ENGLISH
  Document Type: JOURNAL ARTICLE


 3/3/3
DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

01022892   93329041   MEDL/93329041
  Humanized Mik beta 1, a humanized antibody to the IL-2 receptor
beta-chain that acts synergistically with humanized anti-TAC.
  Hakimi J; Ha VC; Lin P; Campbell E; Gately MK; Tsudo M; Payne PW;
Waldmann TA; Grant AJ; Tsien WH; et al
  Roche Research Center, Hoffmann-LaRoche, Inc., Nutley, NJ 07110.
  J Immunol; 151(2):1075-85 1993  ISSN 0022-1767   Journal Code: IFB
  Languages: ENGLISH
  Document Type: JOURNAL ARTICLE
```

3/3/4
DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

01004177 93218273 MEDL/93218273
Cytotoxic activities of recombinant immunotoxins composed of Pseudomonas toxin or diphtheria toxin toward lymphocytes from patients with adult T-cell leukemia.
Kreitman RJ; Chaudhary VK; **Waldmann TA**; Hanchard B; Cranston B; FitzGerald DJ; Pastan I
Laboratory of Molecular Biology, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892.
Leukemia; 7(4):553-62 1993 ISSN 0887-6924 Journal Code: LEU
Languages: ENGLISH
Document Type: JOURNAL ARTICLE

3/3/5
DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

00991310 95606931 ICDB/95606931
Lymphokine receptors: a target for immunotherapy of lymphomas (Meeting abstract).
Waldmann TA
NCI, Bethesda, MD 20892
Non-serial; Fifth International Conference on Malignant Lymphoma, June 9-12, 1993, Lugano, Switzerland, p. 46, 1993.: 1993
Languages: ENGLISH
Document Type: MEETING ABSTRACTS

3/3/6
DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

00985141 93693792 ICDB/93693792
Towards optimal anti-**Tac** antibody dosing in the presence of antigenemia in adult T-cell leukemia-lymphoma (Meeting abstract).
Junghans RP; Goldman CK; Carrasquillo J; Reynolds J; Nelson DL; **Waldmann TA**
New England Deaconess Hosp., Boston, MA 02215
Proc Annu Meet Am Assoc Cancer Res; 34:A2849 1993 ISSN 0197-016X
Languages: ENGLISH
Document Type: MEETING ABSTRACTS
? t s4/3/all

4/3/1
DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

01102643 94325579 MEDL/94325579
Treatment of acute graft-versus-host disease with humanized anti-**Tac**: an antibody that binds to the interleukin-2 receptor.
Anasetti C; Hansen JA; **Waldmann TA**; Appelbaum FR; Davis J; Deeg HJ; Doney K; Martin PJ; Nash R; Storb R; et al
Clinical Research Division, Fred Hutchinson Cancer Research Center 98104.
Blood; 84(4):1320-7 1994 ISSN 0006-4971 Journal Code: A8G
Contract/Grant No.: CA 18029, SS, CA, SS, NCI; CA 18221, SS, CA, SS, NCI; HL36444, SS, HL, SS, NHLBI; +
Languages: ENGLISH
Document Type: JOURNAL ARTICLE

4/3/2

DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

01092742 94266289 MEDL/94266289
Anti-IL-2 receptor monoclonal antibody (anti-**Tac**) treatment of T-cell lymphoma.
Waldmann TA
Metabolism Branch, National Cancer Institute, Bethesda, Maryland.
Important Adv Oncol; :131-41 1994 ISSN 0883-5896 Journal Code: GG9
Languages: ENGLISH
Document Type: JOURNAL ARTICLE; REVIEW; REVIEW, ACADEMIC

4/3/3
DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

01086036 94226936 MEDL/94226936
Lymphokine receptors: a target for immunotherapy of lymphomas.
Waldmann TA
Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.
Ann Oncol; 5 Suppl 1:13-7 1994 ISSN 0923-7534 Journal Code: AYF
Languages: ENGLISH
Document Type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

4/3/4
DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

01083831 94211860 MEDL/94211860
Cooperative interactions between the interleukin 2 receptor alpha and beta chains alter the interleukin 2-binding affinity of the receptor subunits.
Roessler E; Grant A; Ju G; Tsudo M; Sugamura K; **Waldmann TA**
Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892.
Proc Natl Acad Sci U S A; 91(8):3344-7 1994 ISSN 0027-8424 Journal Code: PV3
Languages: ENGLISH
Document Type: JOURNAL ARTICLE
? ds

Set	Items	Description
S1	254	E1,E19
S2	72	S1 AND TAC
S3	6	S2 AND PY=1993
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...completed examining records
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5/3/1
DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

01559550 20021681 MEDL/20021681
Responses in refractory hairy cell leukemia to a recombinant immunotoxin.
Kreitman RJ; Wilson WH; Robbins D; Margulies I; Stetler-Stevenson M; **Waldmann TA**; Pastan I

Laboratory of Molecular Biology, the Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD.
Blood; 94(10):3340-8 1999 ISSN 0006-4971 Journal Code: A8G
Languages: ENGLISH
Document Type: CLINICAL TRIAL; CLINICAL TRIAL, PHASE I; JOURNAL ARTICLE

5/3/2
DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

01516566 99251477 MEDL/99251477
Favorable effects of glycolate conjugation on the biodistribution of humanized antiTac Fab fragment.
Kobayashi H; Kim IS; Drumm D; Kim MK; Paik DS; Le N; **Waldmann TA**; Carrasquillo JA; Paik CH
Department of Nuclear Medicine, Warren G. Magnuson Clinical Center, National Institutes of Health, Bethesda, Maryland 20892-1180, USA.
J Nucl Med; 40(5):837-45 1999 ISSN 0161-5505 Journal Code: JEC
Languages: ENGLISH
Document Type: JOURNAL ARTICLE

5/3/3
DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

01479275 99066764 MEDL/99066764
Reduction in HTLV-I proviral load and spontaneous lymphoproliferation in HTLV-I-associated myelopathy/tropical spastic paraparesis patients treated with humanized anti-**Tac**.
Lehky TJ; Levin MC; Kubota R; Bamford RN; Flerlage AN; Soldan SS; Leist TP; Xavier A; White JD; Brown M; Fleisher TA; Top LE; Light S; McFarland HF ; **Waldmann TA**; Jacobson S
Neuroimmunology Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA.
Ann Neurol; 44(6):942-7 1998 ISSN 0364-5134 Journal Code: 6AE
Languages: ENGLISH
Document Type: JOURNAL ARTICLE

5/3/4
DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

01441042 98301301 MEDL/98301301
Examination of a role for idiotypy in the disease remission of a long-term survivor of adult T cell leukemia treated with anti-**Tac** antibody.
Kingsbury GA; **Waldmann TA**; Junghans RP
Biotherapeutics Development Lab, Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, MA 02115, USA.
Leukemia; 12(6):982-91 1998 ISSN 0887-6924 Journal Code: LEU
Languages: ENGLISH
Document Type: JOURNAL ARTICLE

5/3/5
DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

01436925 98280344 MEDL/98280344
Epitope blocking: positive and negative effects on the biodistribution of 125I-labeled anti-**Tac** disulfide-stabilized Fv fragment of two antibodies against different epitopes of the circulating antigen.
Kobayashi H; Sun BF; Han ES; Kim MK; Le N; Wang QC; Nelson DL; Pastan I;

Waldmann TA; Paik CH; Carrasquillo JA
Department of Nuclear Medicine, Warren G. Magnuson Clinical Center, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892-1180, USA.
Jpn J Cancer Res; 89(4):436-44 1998 ISSN 0910-5050 Journal Code: HBA
Languages: ENGLISH
Document Type: JOURNAL ARTICLE

5/3/6
DIALOG(R)File 159:Cancerlit

01414399 98132664 MEDL/98132664
Impact of antigenemia on the bioactivity of infused anti-**Tac** antibody: implications for dose selection in antibody immunotherapies.
Junghans RP; Carrasquillo JA; **Waldmann TA**
Biotherapeutics Development Lab, Harvard Medical School, Division of Hematology-Oncology, Beth Israel Deaconess Medical Center, Boston, MA 02115, USA. junghans@warren.med.harvard.edu
Proc Natl Acad Sci U S A; 95(4):1752-7 1998 ISSN 0027-8424 Journal Code: PV3
Languages: ENGLISH
Document Type: JOURNAL ARTICLE

5/3/7
DIALOG(R)File 159:Cancerlit

01353147 97301590 MEDL/97301590
Improved biodistribution of 125I-labeled anti-**Tac** disulfide-stabilized Fv fragment by blocking its binding to the alpha subunit of the interleukin 2 receptor in the circulation with preinjected humanized anti-**Tac** IgG.
Kobayashi H; Yoo TM; Drumm D; Kim MK; Sun BF; Le N; Webber KO; Pastan I; **Waldmann TA**; Paik CH; Carrasquillo JA
Department of Nuclear Medicine, National Cancer Institute, NIH, Bethesda, Maryland 20892-1180, USA.
Cancer Res; 57(10):1955-61 1997 ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH
Document Type: JOURNAL ARTICLE

5/3/8
DIALOG(R)File 159:Cancerlit

01326403 98641089 ICDB/98641089
Phase I clinical trial with recombinant immunotoxin anti-**Tac** (Fv)-PE38 (LMB-2) in patients with hematologic malignancies (Meeting abstract).
Kreitman RJ; White JD; Pearson D; Top LE; **Waldmann TA**; Pastan I
National Cancer Institute, National Institutes of Health, Bethesda, MD 20892-4255
Proc Annu Meet Am Assoc Cancer Res; 38:A4089 1997 ISSN 0197-016X
Languages: ENGLISH
Document Type: MEETING ABSTRACTS; CLINICAL TRIAL; CLINICAL TRIAL, PHASE I

5/3/9
DIALOG(R)File 159:Cancerlit

01281441 96390748 MEDL/96390748
The promiscuous IL-2/IL-15 receptor: a target for immunotherapy of

HTLV-I-associated disorders.
Waldmann TA
Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
J Acquir Immune Defic Syndr Hum Retrovirol; 13 Suppl 1:S179-85 1996
ISSN 1077-9450 Journal Code: B7J
Languages: ENGLISH
Document Type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

5/3/10
DIALOG(R)File 159:Cancerlit

01261511 96261660 MEDL/96261660
Metabolism of **Tac** (IL2Ralpha): physiology of cell surface shedding and renal catabolism, and suppression of catabolism by antibody binding.
Junghans RP; **Waldmann TA**
Division of Hematology-Oncology, Harvard Medical School, New England Deaconess Hospital, Boston, MA 02215, USA.
J Exp Med; 183(4):1587-602 1996 ISSN 0022-1007 Journal Code: I2V
Languages: ENGLISH
Document Type: JOURNAL ARTICLE

5/3/11
DIALOG(R)File 159:Cancerlit

01213309 96082159 MEDL/96082159
Radioimmunotherapy of interleukin-2R alpha-expressing adult T-cell leukemia with Yttrium-90-labeled anti-**Tac** [see comments]
Waldmann TA; White JD; Carrasquillo JA; Reynolds JC; Paik CH; Gansow OA; Brechbiel MW; Jaffe ES; Fleisher TA; Goldman CK; et al
Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.
Blood; 86(11):4063-75 1995 ISSN 0006-4971 Journal Code: A8G
Comment in SS Blood SS 1996 Jun 15;87(12):5379-80
Languages: ENGLISH
Document Type: CLINICAL TRIAL; CLINICAL TRIAL, PHASE I; CLINICAL TRIAL, PHASE II; JOURNAL ARTICLE

5/3/12
DIALOG(R)File 159:Cancerlit

01170001 95241460 MEDL/95241460
Phenotypic knockout of the high-affinity human interleukin 2 receptor by intracellular single-chain antibodies against the alpha subunit of the receptor.
Richardson JH; Sodroski JG; **Waldmann TA**; Marasco WA
Department of Pathology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA 02115, USA.
Proc Natl Acad Sci U S A; 92(8):3137-41 1995 ISSN 0027-8424
Journal Code: PV3
Contract/Grant No.: P30 AI28691, SS, AI, SS, NIAID; P30 CA06516, SS, CA, SS, NCI; AI28785, SS, AI, SS, NIAID; +
Languages: ENGLISH
Document Type: JOURNAL ARTICLE

5/3/13
DIALOG(R)File 159:Cancerlit

01156141 97609760 ICDB/97609760
The promiscuous IL-2 receptor: a target for immunotherapy of HTLV-I-associated diseases (Meeting abstract).
Waldmann TA
Metabolism Branch, NCI, NIH Bethesda, MD 20892
Int J Oncol; 7(Suppl):980 1995 ISSN 1019-6439
Languages: ENGLISH
Document Type: MEETING ABSTRACTS

5/3/14
DIALOG(R)File 159:Cancerlit
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01102643 94325579 MEDL/94325579
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Languages: ENGLISH
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Contract/Grant No.: CA-28149, SS, CA, SS, NCI
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Pseudomonas exotoxin-anti-**TAC** . Cell-specific immunotoxin active

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00357793 83601683 ICDB/83601683
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Department of Hematology and Oncology, Medizinische Hochschule Hanover, Germany.
Cancer Res; 51(23 Pt 1):6312-6 1991 ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH

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 s tac and lymphoma?

            1376  TAC
           79436  LYMPHOMA?
      S6     168  TAC AND LYMPHOMA?
? s s6 and py=1993

             168  S6
           80574  PY=1993
      S7      12  S6 AND PY=1993
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...completed examining records
      S8      12  RD S7 (unique items)
? s s6 and py=1994

             168  S6
           83740  PY=1994
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01040145   94036762   MEDL/94036762
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01034122   94003208   MEDL/94003208
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  Languages: ENGLISH
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01019871 93311229 MEDL/93311229
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01004177 93218273 MEDL/93218273
Cytotoxic activities of recombinant immunotoxins composed of Pseudomonas toxin or diphtheria toxin toward lymphocytes from patients with adult T-cell leukemia.
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00986602 94690741 ICDB/94690741
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Languages: ENGLISH
Document Type: MEETING ABSTRACTS

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Junghans RP; Goldman CK; Carrasquillo J; Reynolds J; Nelson DL; Waldmann TA
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Languages: ENGLISH
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Foss F; Borkowski T; Tompkins A; Gilliom M; Cooper M; Udey M; Stetler-Stevenson M; Jaffe E; Woodworth T; Sausville E
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Languages: ENGLISH
Document Type: MEETING ABSTRACTS
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01138480 95182475 MEDL/95182475
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01109205 94362224 MEDL/94362224
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Languages: ENGLISH
Document Type: CLINICAL TRIAL; CLINICAL TRIAL, PHASE II; JOURNAL ARTICLE

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01102721 94325831 MEDL/94325831
Down-regulation of CD3 antigen on adult T cell leukemia cells.
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Third Department of Internal Medicine, Kinki University School of Medicine, Osaka, Japan.
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Languages: ENGLISH
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01102643 94325579 MEDL/94325579
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Clinical Research Division, Fred Hutchinson Cancer Research Center 98104.
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Contract/Grant No.: CA 18029, SS, CA, SS, NCI; CA 18221, SS, CA, SS, NCI; HL36444, SS, HL, SS, NHLBI; +
Languages: ENGLISH
Document Type: JOURNAL ARTICLE

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01101755 94320068 MEDL/94320068
Radioimmunotherapy of nude mice bearing a human interleukin 2 receptor alpha-expressing **lymphoma** utilizing the alpha-emitting radionuclide-conjugated monoclonal antibody 212Bi-anti-**Tac**.
Hartmann F; Horak EM; Garmestani K; Wu C; Brechbiel MW; Kozak RW; Tso J; Kosteiny SA; Gansow OA; Nelson DL; et al
Metabolism Branch, National Cancer Institute, NIH, Bethesda, Maryland 20892.
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01097860 94297519 MEDL/94297519
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Kreitman RJ; Pastan I
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Languages: ENGLISH
Document Type: JOURNAL ARTICLE; REVIEW; REVIEW, ACADEMIC

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01092742 94266289 MEDL/94266289
Anti-IL-2 receptor monoclonal antibody (anti-**Tac**) treatment of T-cell **lymphoma**.
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01089877 94249675 MEDL/94249675
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Languages: ENGLISH
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01071386 96605013 ICDB/96605013
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Division of Hematology/Oncology and Department of Pathology, Wayne State University, Detroit, MI
Blood; 84(10, Suppl 1):374a 1994 ISSN 0903-1936
Languages: ENGLISH
Document Type: MEETING ABSTRACTS
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Set     Items   Description
S1        254   E1,E19
S2         72   S1 AND TAC
S3          6   S2 AND PY=1993
S4          4   S2 AND PY=1994
S5         69   RD S2 (unique items)
S6        168   TAC AND LYMPHOMA?
S7         12   S6 AND PY=1993
S8         12   RD S7 (unique items)
S9         10   S6 AND PY=1994
? s s6 and soluble(10n)(IL(w)2 or IL(w)2R)

            168  S6
          20463  SOLUBLE
          61351  IL
         499237  2
          21778  IL(W)2
          61351  IL
           3103  2R
           2251  IL(W)2R
            826  SOLUBLE(10N)(IL(W)2 OR IL(W)2R)
    S10       5  S6 AND SOLUBLE(10N)(IL(W)2 OR IL(W)2R)
? rd s10

...completed examining records
    S11       5  RD S10 (unique items)
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s soluble(30n)(IL(w)2 or IL(w)2R or IL(w)2(w)receptor?) and tac

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           61351  IL
          499237  2
           21778  IL(W)2
           61351  IL
            3103  2R
            2251  IL(W)2R
           61351  IL
          499237  2
          122702  RECEPTOR?
            3467  IL(W)2(W)RECEPTOR?
            1164  SOLUBLE(30N)((IL(W)2 OR IL(W)2R) OR IL(W)2(W)RECEPTOR?)
            1376  TAC
     S12      43  SOLUBLE(30N)(IL(W)2 OR IL(W)2R OR IL(W)2(W)RECEPTOR?) AND
                  TAC
? rd s12

...completed examining records
     S13      43  RD S12 (unique items)
? t s13/3/all


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01095932   94286643   MEDL/94286643
  Targeting human IL-2 receptors for diagnosis and therapy.
  Nelson DL; Kurman CC
  Immunophysiology  Section, National Cancer Institute, National Institutes
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  Proc Soc Exp Biol Med; 206(3):309-11 1994  ISSN 0037-9727
Journal Code: PXZ
  Languages: ENGLISH
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01075134   94139113   MEDL/94139113
   Follow  up  of  soluble  IL-2  receptor level in
metastatic malignant melanoma patients treated by chemoimmunotherapy.
  Soubrane  C;  Mouawad  R;  Ichen  M;  Suissa  J;  Borel  C;  Vuillemin E;
Benhammouda A; Bizzari JP; Weil M; Khayat D
  Department of Medical Oncology, Salpetriere Hospital, Paris, France.
  Clin Exp Immunol; 95(2):232-6 1994  ISSN 0009-9104   Journal Code: DD7
  Languages: ENGLISH
  Document Type: JOURNAL ARTICLE


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01073616   94118567   MEDL/94118567
  Does  IL-2  receptor  expression and secretion in chronic B-cell leukemia
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have a role in down-regulation of the immune system?
Burton J; Kay NE
Metabolism Branch, National Institute of Health, Bethesda, MD.
Leukemia; 8(1):92-6 1994 ISSN 0887-6924 Journal Code: LEU
Languages: ENGLISH
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01049259 94092956 MEDL/94092956
Human T lymphocyte activation by pokeweed mitogen induces production of TNF-alpha and GM-CSF and helper signaling by IL-1 and IL-6 results in IL-2-dependent T cell growth.
Wallays G; Ceuppens JL
Department of Medicine and Pathophysiology, University of Leuven, Belgium.
Eur Cytokine Netw; 4(4):269-77 1993 ISSN 1148-5493 Journal Code: A56
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01034189 94003317 MEDL/94003317
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Kondo A; Imada K; Hattori T; Yamabe H; Tanaka T; Miyasaka M; Okuma M; Uchiyama T
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00966791 93077183 MEDL/93077183
Chemo-immunotherapy in patients with metastatic melanoma using sequential treatment with dacarbazine and recombinant human interleukin-2: evaluation of hematologic and immunologic parameters and correlation with clinical response.
Isacson R; Kedar E; Barak V; Gazit Z; Yurim O; Kalichman I; Ben-Bassat H; Biran S; Schlesinger M; Franks CR; et al
Department of Oncology, Hadassah University Hospital, Jerusalem, Israel.
Immunol Lett; 33(2):127-34 1992 ISSN 0165-2478 Journal Code: GIH
Languages: ENGLISH
Document Type: CLINICAL TRIAL; CLINICAL TRIAL, PHASE II; JOURNAL ARTICLE; MULTICENTER STUDY

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00950624 92388287 MEDL/92388287
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Protein Biochemistry Department, Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ 07110.

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00930410 92256201 MEDL/92256201
Diagnostic and clinical importance of interleukin-2 receptor alpha chain expression on non-T-cell acute leukaemia cells.
Nakase K; Kita K; Otsuji A; Anazawa H; Hoshino K; Sekine T; Shirakawa S; Tanaka I; Nasu K; Tsutani H; et al
Second Department of Internal Medicine, Faculty of Medicine, Mie University, Tsu, Japan.
Br J Haematol; 80(3):317-26 1992 ISSN 0007-1048 Journal Code: AXC
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00924210 92208969 MEDL/92208969
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Pizzolo G; Vincenzi C; Vinante F; Rigo A; Veneri D; Chilosi M; Dusi S; Poli G; Zambello R; Semenzato G; et al
Cattedra di Ematologia, Istituto di Patologia Generale, Verona, Italy.
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00923445 92201878 MEDL/92201878
The monocyte interleukin-2 receptor light chain: production of cell-associated and soluble interleukin-2 receptor by monocytes.
Kniep EM; Strelow I; Lohmann-Matthes ML
Abteilung fur Immunobiologie, Fraunhofer Institut fur Toxikologie, Hannover, Germany.
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00914263 93689708 ICDB/93689708
Combination of rIFN alpha-2a and IL-2 in melanoma patients: what are effective doses? (Meeting abstract).
Castello G; Comella P; Napolitano M; Manzo T; Leonardi E; Galati MG; Casaretti R; Daponte A; Comella G
Natl. Cancer Inst. of Naples, Naples, Italy
Ann Oncol; 3(Suppl 5):141 1992 ISSN 0923-7534
Languages: ENGLISH
Document Type: MEETING ABSTRACTS; CLINICAL TRIAL

13/3/12
DIALOG(R)File 159:Cancerlit
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00903052 92136003 MEDL/92136003
The cytokine receptor superfamily.
Kaczmarski RS; Mufti GJ
Department of Haematological Medicine, King's College School of Medicine and Dentistry, London, UK.
Blood Rev; 5(3):193-203 1991 ISSN 0268-960X Journal Code: BLR
Languages: ENGLISH
Document Type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

13/3/13
DIALOG(R)File 159:Cancerlit
(c) format only 2000 Dialog Corporation. All rts. reserv.

00889575 92034763 MEDL/92034763
Biological monitoring of low-dose interleukin 2 in humans: soluble interleukin 2 receptors, cytokines, and cell surface phenotypes.
Hanninen EL; Korfer A; Hadam M; Schneekloth C; Dallmann I; Menzel T; Kirchner H; Poliwoda H; Atzpodien J
Department of Hematology and Oncology, Medizinische Hochschule Hanover, Germany.
Cancer Res; 51(23 Pt 1):6312-6 1991 ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH
Document Type: JOURNAL ARTICLE

13/3/14
DIALOG(R)File 159:Cancerlit
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00881013 91360958 MEDL/91360958
[The interleukin-2 receptor (editorial)]
Il recettore dell'interleukina-2.
Marino P; Preatoni A
Recenti Prog Med; 82(5):291-3 1991 ISSN 0034-1193 Journal Code: R1T
Languages: ITALIAN
Document Type: EDITORIAL English Abstract

13/3/15
DIALOG(R)File 159:Cancerlit
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00819435 91002416 MEDL/91002416
Increased serum levels of **soluble IL-2 receptor**, CD30 and CD8 molecules, and gamma-interferon in angioimmunoblastic lymphadenopathy: possible pathogenetic role of immunoactivation mechanisms.
Pizzolo G; Stein H; Josimovic-Alasevic O; Vinante F; Zanotti R; Chilosi M ; Feller AC; Diamantstein T
Department of Hematology, Verona University, Italy.
Br J Haematol; 75(4):485-8 1990 ISSN 0007-1048 Journal Code: AXC
Languages: ENGLISH
Document Type: JOURNAL ARTICLE

Article title	The use of antibodies against the IL-2 receptor in transplantation
Article identifier	0952791598003542
Authors	Waldmann_T_A O'Shea_J
Journal title	Current Opinion in Immunology
ISSN	0952-7915
Publisher	Current Biology
Year of publication	1998
Volume	10
Issue	5
Supplement	0
Page range	507-512
Number of pages	6
User name	Adonis
Cost centre	Development
PCC	$20.00
Date and time	Thursday, March 09, 2000 12:35:16 AM

2/3/53 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

111005761 CA: 111(1)5761u PATENT
Monoclonal antibody to Tac receptor for treatment of malignancy and autoimmune disorders in humans
INVENTOR(AUTHOR): Waldmann, T. A.
LOCATION: USA
ASSIGNEE: United States Dept. of Health and Human Services
PATENT: U.S. Pat. Appl. ; US 85707 A0 DATE: 880415
APPLICATION: US 85707 (870817)
PAGES: 18 pp. Avail. NTIS Order No. PAT-APPL-7-85707. CODEN: XAXXAV

2/3/52 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

117190132 CA: 117(19)190132z PATENT
Antibody composition directed against human or animal interleukin-2 (IL-2) receptor, and therapeutic uses thereof
INVENTOR(AUTHOR): Jacques, Yannick; Soulillou, Jean Paul; Audrain, Marie; Francois-Bendahou, Christine
LOCATION: Fr.
ASSIGNEE: Institut National de la Sante et de la Recherche Medicale (INSERM)
PATENT: PCT International ; WO 9213886 A1 DATE: 920820
APPLICATION: WO 92FR75 (920128) *FR 911102 (910131)
PAGES: 30 pp. CODEN: PIXXD2 LANGUAGE: French CLASS: C07K-015/00A
DESIGNATED COUNTRIES: AU; CA; JP; KR; US DESIGNATED REGIONAL: AT; BE; CH ; DE; DK; ES; FR; GB; GR; IT; LU; MC; NL; SE

2/3/53 (Item 4 from file: 399)

2/3/29 n 1 from file: 73)
DIALOG(R)Fi 3:EMBASE
(c) 2000 El c Science B.V. All rts. reserv.

10828958 \SE No: 2000309668
Successfu /ivo blockade of CD25 (high-affinity interleukin 2
receptor) o ells by administration of humanized anti-**Tac**
antibody to nts with psoriasis
Krueger J Valters I.B.; Miyazawa M.; Gilleaudeau P.; Hakimi J.; Light
S.; Sherr A tlieb A.B.
Dr. J.G. r, Laboratory Head, Rockefeller University, Lab. for
Investiga Dermatology, 1230 York Ave, New York, NY 10021-6399 United
States
AUTHOR EM kruegej@rockvax.rockefeller.edu
Journal o American Academy of Dermatology (J. AM. ACAD. DERMATOL.)
(United Sta 2000, 43/3 (448-458)
CODEN: JA ISSN: 0190-9622
DOCUMENT Journal; Article
LANGUAGE: ISH SUMMARY LANGUAGE: ENGLISH

10828958 EMBASE)0309668
Successful in vivc ıde of CD25 (high-affinity interleukin 2
receptor) on T cells ıinistration of humanized anti-**Tac**
antibody to patients ›soriasis
Krueger J.G.; Walt 3.; Miyazawa M.; Gilleaudeau P.; Hakimi J.; Light
S.; Sherr A.; Gottli .
Dr. J.G. Krueger, :ory Head, Rockefeller University, Lab. for
Investigative Derm ', 1230 York Ave, New York, NY 10021-6399 United
States
AUTHOR EMAIL: krue :kvax.rockefeller.edu
Journal of the Ame ıcademy of Dermatology (J. AM. ACAD. DERMATOL.)
(United States) 20((448-458)
CODEN: JAADD ISS -9622
DOCUMENT TYPE: Jou ırticle
LANGUAGE: ENGLISH ıRY LANGUAGE: ENGLISH
NUMBER OF REFERENC

Background: Dacliz a humanized **antibody** to the alpha-subunit
(CD25) of the interl (**IL-2**) **receptor** that blocks
normal IL-2 binding receptor. Because IL-2 is a major stimulus for
T-cell growth, **block** the **IL-2 receptor** could
be useful in treatir l-mediated (**autoimmune**) diseases.
Objective: Our purpc to determine whether adequate concentrations of
antibody were achiev irculating blood and in psoriatic skin
lesions to saturate ceptors. We also intended to measure clinical
effect and safety of gent when used alone (without other
immunosuppressive dr psoriasis. Methods: Nineteen patients with
psoriasis in two cer ceived daclizumab at an initial dose of 2 mg/kg,
then 1 mg/kg at week 8, and 12. To determine whether CD25 was
blocked in vivo, flc ıetric studies measured (1) expression of CD25 on
CD3sup + T cells der om blood and (2) immunohistochemistry measures
of CD25sup + cells c pretreatment and posttreatment biopsy specimens.
Patients were follow linically with photographs and Psoriasis Area
and Severity Index s Results: This study showed a consistent blockade
of CD25 in peripher and tissue during the first 4 weeks of therapy
while the dosing was 2 weeks. Variable desaturation of receptors
began after 4 weeks, correlated with a reversal in disease
improvement. Patient a pretreatment Psoriasis Area and Severity Index
score of less than 3 d a mean reduction in severity by 30% at 8 weeks
(P = .02). During th eks of treatment, a 44.8% decrease in expression
of the IL-2 receptor subunit was found. The absolute T-cell counts
were calculated and no significant changes during the course of the
study No significant e events were produced by daclizumab during this
study. Conclusion: W fore conclude that daclizumab is a
well-tolerated agent locks CD25 expression in peripheral blood and
skin. Furthermore, i e useful in treating psoriasis in some patients.

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     53   RD S1 (uni          ns)
? s s2 and (soluble)          (w)2R or receptor?)

             53  S2
         326299  SO
         256953  IL
          21117  2R
           8771  IL
        1948284  RE
          19857  SO          N)(IL(W)2R OR RECEPTOR?)
S3            0  S2          OLUBLE)(5N)(IL(W)2R OR RECEPTOR?)
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S  - DIALOG OneSearch
  File   5:Biosis Previews(R)  1969-2001/Jul W1
         (c) 2001 BIOSIS
  File  73:EMBASE  1974-2001/Jun W4
         (c) 2001 Elsevier Science B.V.
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         (c) format only 2001 Dialog Corporation
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  File 399:CA SEARCH(R)  1967-2001/UD=13501
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      Set   Items  Description
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? e au=waldmann thomas ?


Ref    Items  Index-term
E1         3  AU=WALDMANN TH.
E2        12  AU=WALDMANN THOMAS
E3         0 *AU=WALDMANN THOMAS ?
E4        65  AU=WALDMANN THOMAS A
E5         1  AU=WALDMANN THOMAS ALEXANDER
E6         1  AU=WALDMANN THOMAS W
E7         1  AU=WALDMANN TODD B
E8         2  AU=WALDMANN TODD M
E9         1  AU=WALDMANN TS
E10       15  AU=WALDMANN U
E11        7  AU=WALDMANN U.
E12        1  AU=WALDMANN ULRICH

          Enter P or PAGE for more
? s e1-e5

               3  AU=WALDMANN TH.
              12  AU=WALDMANN THOMAS
               0  AU=WALDMANN THOMAS ?
              65  AU=WALDMANN THOMAS A
               1  AU=WALDMANN THOMAS ALEXANDER
      S1      81  E1-E5
? rd s1

...examined 50 records  (50)
...completed examining records
      S2      79  RD S1 (unique items)
? s s2 and tac

              79  S2
            9383  TAC
      S3      25  S2 AND TAC
? t s3/7/all


 3/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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13107907 BIOSIS NO.: 200100315056
Pretargeting radioimmunotherapy with the alpha emitter, BI-213, in the treatment of adult T cell leukemia (ATL).
AUTHOR: Zhang Meili(a); Yao Zhengsheng; Garmestani Kayhan; Axworthy Donald B; Mallett Robert W; Fritzberg Alan R; Brechbiel Martin W; Carrasquillo Jorge A; **Waldmann Thomas A**(a
AUTHOR ADDRESS: (a)Metabolism Branch, National Cancer Institute, NIH, Bethesda, MD**USA
JOURNAL: Blood 96 (11 Part 1):p721a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Adult T-cell leukemia (ATL) consists of an overabundance of activated T cells which are characterized by the expression of CD25 or IL-2Ralpha on the cell surface. Presently, there is no accepted curative therapy for ATL. In this study, we investigated the use of a pretargeting technique with the alpha-emitter, Bi-213, to treat ATL. DOTA-biotin was labeled with Bi-213 at a specific activity of >1 mCi/mug. Humanized anti-**Tac** antibody (HAT), which recognizes CD25, was conjugated to streptavidin (SA) forming HAT-SA. A tumor model was established by i.p. injection of 20X106 tumor cells from human ATL-tumor bearing mice into NOD/SCID mice. The therapy study was performed at two weeks after the inoculation. Before therapy and every two weeks thereafter, serum soluble **Tac** (sIL-2Ralpha) levels were measured in order to monitor tumor growth. HAT-SA (140 mug) was used allowing pretargeting for 24 hours. Then, 100 mug of synthetic clearing agent (sCA), containing biotin and galactose arms, developed by NeoRx, was used to clear unbound conjugate from the circulation. Four hours later, 0.3 mug of Bi-213 labeled DOTA-biotin was given for therapy. Groups of 5 mice each were treated with 0, 50, 150, 250 or 350 muCi of Bi-213 and one group without any treatment served as a control. Complete blood count (CBC) was monitored for toxicity weekly. Results: The tumor growth was inhibited by using 250 or 350 muCi of Bi-213 labeled biotin in the pretargeting technique as indicated by the significant reduction of sIL-2Ralpha levels ($p<0.005$, t test) compared with the control group on day 28. Furthermore, there was a significant prolongation of the survival of the mice treated with either 250 or 350 muCi of Bi-213 as compared with the control group ($p<0.02$, rank test). The median survival duration of the control group was 52 days, whereas it increased to >75.6 and >67 days in 250 and 350 muCi Bi-213 treated groups, respectively. The CBC results revealed a dose dependant decrease of platelet and white blood cell count one week after therapy, with recovery three weeks later. Conclusion: Bi-213 labeled biotin used with the pretargeting technique proved to be an effective therapeutic for ATL without unacceptable toxicity.

3/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12862062 BIOSIS NO.: 200100069211
IL-2Ralpha-directed monoclonal antibodies provide effective therapy in a murine model of adult T-cell leukemia by a mechanism other than blockade of IL-2/IL-2Ralpha interaction.
AUTHOR: Phillips Kathleen E; Herring Bert; Wilson Latresia A; Rickford Marc S; Zhang Meili; Goldman Carolyn K; Tso J Yun; **Waldmann Thomas A**(a
AUTHOR ADDRESS: (a)Metabolism Branch, National Cancer Institute, NIH, 10 Center Drive, Building 10, Room 4N-115, Bethesda, MD, 20892-1374**USA
JOURNAL: Cancer Research 60 (24):p6977-6984 December 15, 2000

MEDIUM: print
ISSN: 0008-5472
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Adult T-cell leukemia (ATL) develops in a small proportion of human T-cell lymphotrophic virus-I infected individuals. The leukemia consists of an overabundance of activated T cells, which are characterized by the expression of CD25, or IL-2Ralpha, on their cell surface. Presently, there is not an accepted curative therapy for ATL. We developed an in vivo model of ATL in non-obese diabetic/severe combined immunodeficient (NOD/SCID) mice by introducing cells from an ATL patient (MET-1) into the mice. The leukemic cells proliferated in these mice that lack functional T, B, and natural killer (NK) cells. The MET-1 leukemic cells could be monitored by measurements of both serum soluble **Tac** (IL-2Ralpha) and soluble human beta2-microglobulin (beta2mu) by ELISA. The disease progressed to death in the mice after apprx4-6 weeks. The mice developed grossly enlarged spleens and a leukemia involving ATL cells that retained the phenotype and the T-cell receptor rearrangement and human T-cell lymphotrophic virus-I integration pattern of the patient's ATL leukemia cells. This model is of value for testing the efficacy of novel therapeutic agents for ATL. The administration of humanized anti-**Tac** (HAT), murine anti-**Tac** (MAT), and 7G7/B6, all of which target IL-2Ralpha, significantly delayed the progression of the leukemia and prolonged the survival of the tumor-bearing mice. In particular, HAT induced complete remissions in 4 of 19 mice and partial remissions in the remainder. It appears that the antibodies act by a mechanism that had not been anticipated. The prevailing view is that antibodies to the IL-2Ralpha receptor have their effective action by blocking the interaction of IL-2 with its growth factor receptor, thereby inducing cytokine deprivation apoptosis. However, although both HAT and MAT block the binding of IL-2 to IL-2Ralpha of the high affinity receptor, the 7G7/B6 monoclonal antibody binds to a different epitope on the IL-2Ralpha receptor, one that is not involved in IL-2 binding. This suggested that the antibodies provide an effective therapy by a mechanism other than induction of cytokine deprivation. In accord with this view, the MET-1 cells obtained from the spleens of leukemic mice did not produce IL-2, nor did they express IL-2 mRNA as assessed by reverse transcription-PCR. Another possible conventional mechanism of action involves complement-mediated killing. However, although MAT and 7G7/B6 fix rabbit complement, HAT does not do so. Furthermore, in the presence of NOD/SCID mouse serum, there was no complement-mediated lysis of MET-1 cells. In addition, the antibodies did not manifest antibody-dependent cellular cytotoxicity with NOD/SCID splenocytes that virtually lack NK cells as the effector cells as assessed in an in vitro chromium-release assay. However, in contrast to the efficacy of intact HAT, the F(ab')2 version of this antibody was not effective in prolonging the survival of mice injected with MET-1 ATL cells. In conclusion, in our murine model of ATL, monoclonal antibodies, HAT, MAT, and 7G7/B6, appear to delay progression of the leukemia by a mechanism of action that is different from the accepted mechanism of IL-2 deprivation leading to cell death. We consider two alternatives: the first, antibody-dependent cellular cytotoxicity mediated by FcRI- or FcRIII-expressing cells other than NK cells, such as monocytes or polymorphonuclear leukocytes. The second alternative we consider involves direct induction of apoptosis by the anti-IL-2R antibodies in vivo. It has been shown that the IL-2R is a critical element in the peripheral self-tolerance T-cell suicide mechanism involved in the phenomenon of activation-induced cell death.

3/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12831477 BIOSIS NO.: 200100038626
Advances in interleukin 2 receptor targeted treatment.
AUTHOR: Morris John C(a); **Waldmann Thomas A**
AUTHOR ADDRESS: (a)Metabolism Branch, Division of Clinical Sciences, National Cancer Institute, NIH, 10 Center Drive, Bldg 10, Rm 4N115, Bethesda, MD, 20892-1374: jmorris@mail.nih.gov**USA
JOURNAL: Annals of the Rheumatic Diseases 59 (Supplement 1):pi109-i114 November, 2000
MEDIUM: print
ISSN: 0003-4967
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: T cell activation and cellular immune responses are modulated by interleukin 2 (IL2) through binding to its corresponding cell surface receptor. Three forms of the receptor are recognised based on IL2 binding affinity. The high affinity receptor is a heterotrimer composed of alpha, beta, and gammac-polypeptide chains. The 55 kDa alpha-chain also known as the **Tac** (T cell activation) antigen or CD-25 is a unique subunit of the high affinity IL2 receptor (IL2Ralpha). Resting T cells express few IL2Ralpha, however, when activated, the expression of ILR2alpha rapidly increases. The IL2Ralpha is shed from the cell surface and is measurable in the serum as a 45 kDa soluble form (s-**Tac** or s-IL2Ralpha). Serum concentrations of s-**Tac** can be used as a surrogate marker for T cell activation and IL2Ralpha expression. IL2Ralpha is over expressed by T cells in a number of autoimmune diseases, allograft rejection and a variety of lymphoid neoplasms. IL2 induced proliferation of T cells can be inhibited by the murine monoclonal antibody (anti-**Tac**) directed against the alpha-chain of the IL2R. Through molecular engineering, murine anti-**Tac** has been humanised reducing its immunogenicity without changing its specificity. Humanised anti-**Tac** (HAT) has been shown to reduce the incidence of renal and cardiac allograft rejection as well as decrease the severity of graft versus host disease in patients undergoing HLA matched allogeneic bone marrow transplantation. IL2Ralpha targeted treatment with radioimmunoconjugates of anti-**Tac** and immunotoxins has shown promise in the treatment of CD25 expressing lymphomas.

3/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12482143 BIOSIS NO.: 200000235645
Phase I trial of recombinant immunotoxin anti-**Tac**(Fv)-PE38 (LMB-2) in patients with hematologic malignancies.
AUTHOR: Kreitman Robert J; Wilson Wyndham H; White Jeffrey D; Stetler-Stevenson Maryalice; Jaffe Elaine S; Giardina Steven; **Waldmann Thomas A**; Pastan Ira(a
AUTHOR ADDRESS: (a)Laboratory of Molecular Biology, National Cancer Institute, National Institute of Health, 9000 Rockville Pike, Building 37/4E16, Bethesda, MD, 20892**USA
JOURNAL: Journal of Clinical Oncology 18 (8):p1622-1636 April, 2000
ISSN: 0732-183X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Purpose: To evaluate the toxicity, pharmacokinetics, immunogenicity, and antitumor activity of anti-**Tac**(Fv)-PE38 (LMB-2), an anti-CD25 recombinant immunotoxin that contains an antibody Fv fragment fused to truncated Pseudomonas exotoxin. Patients and Methods: Patients with CD25+ hematologic malignancies for whom standard

and salvage therapies failed were treated with LMB-2 at dose levels that ranged from 2 to 63 mug/kg administered intravenously over 30 minutes on alternate days for three doses (QOD X 3). Results: LMB-2 was administered to 35 patients for a total of 59 cycles. Dose-limiting toxicity at the 63 mug/kg level was reversible and included transaminase elevations in one patient and diarrhea and cardiomyopathy in another. LMB-2 was well tolerated in nine patients at the maximum-tolerated dose (40 mug/kg QOD X 3); toxicity was transient and most commonly included transaminase elevations (eight patients) and fever (seven patients). Only six of 35 patients developed significant neutralizing antibodies after the first cycle. The median half-life was 4 hours. One hairy cell leukemia (HCL) patient achieved a complete remission, which is ongoing at 20 months. Seven partial responses were observed in cutaneous T-cell lymphoma (one patient), HCL (three patients), chronic lymphocytic leukemia (one patient), Hodgkin's disease (one patient), and adult T-cell leukemia (one patient). Responding patients had 2 to 5 log reductions of circulating malignant cells, improvement in skin lesions, and regression of lymphomatous masses and splenomegaly. All four patients with HCL responded to treatment. Conclusion: LMB-2 has clinical activity in CD25+ hematologic malignancies and is relatively nonimmunogenic. It is the first recombinant immunotoxin to induce major responses in cancer. LMB-2 and similar agents that target other cancer antigens merit further clinical development.

12831477 BIOSIS NO.: 200100038626
Advances in interleukin 2 receptor targeted treatment.
AUTHOR: Morris John C(a); **Waldmann Thomas A**
AUTHOR ADDRESS: (a)Metabolism Branch, Division of Clinical Sciences, National Cancer Institute, NIH, 10 Center Drive, Bldg 10, Rm 4N115, Bethesda, MD, 20892-1374: jmorris@mail.nih.gov**USA
JOURNAL: Annals of the Rheumatic Diseases 59 (Supplement 1):pi109-i114 November, 2000
MEDIUM: print
ISSN: 0003-4967
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: T cell activation and cellular immune responses are modulated by interleukin 2 (IL2) through binding to its corresponding cell surface receptor. Three forms of the receptor are recognised based on IL2 binding affinity. The high affinity receptor is a heterotrimer composed of alpha, beta, and gammac-polypeptide chains. The 55 kDa alpha-chain also known as the **Tac** (T cell activation) antigen or CD-25 is a unique subunit of the high affinity IL2 receptor (IL2Ralpha). Resting T cells express few IL2Ralpha, however, when activated, the expression of ILR2alpha rapidly increases. The IL2Ralpha is shed from the cell surface and is measurable in the serum as a 45 kDa soluble form (s-**Tac** or s-IL2Ralpha). Serum concentrations of s-**Tac** can be used as a surrogate marker for T cell activation and IL2Ralpha expression. IL2Ralpha is over expressed by T cells in a number of autoimmune diseases, allograft rejection and a variety of lymphoid neoplasms. IL2 induced proliferation of T cells can be inhibited by the murine monoclonal antibody (anti-**Tac**) directed against the alpha-chain of the IL2R. Through molecular engineering, murine anti-**Tac** has been humanised reducing its immunogenicity without changing its specificity. Humanised anti-**Tac** (HAT) has been shown to reduce the incidence of renal and cardiac allograft rejection as well as decrease the severity of graft versus host disease in patients undergoing HLA matched allogeneic bone marrow transplantation. IL2Ralpha targeted treatment with radioimmunoconjugates of anti-**Tac** and immunotoxins has shown promise in the treatment of CD25 expressing lymphomas.

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? s (tac)(10n)(antibod?)(30n)(radiolabel? or yttrium? or
90Y)(40n)(mg)(40n)(treat? or therap? or administ?)

Processing
Processing
Processing
          8865  TAC
       1537832  ANTIBOD?
         92472  RADIOLABEL?
         81886  YTTRIUM?
          1178  90Y
       1234664  MG
       4863111  TREAT?
       4576406  THERAP?
       2662304  ADMINIST?
     S1       8  (TAC)(10N)(ANTIBOD?)(30N)(RADIOLABEL? OR YTTRIUM? OR
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...completed examining records
     S2       3  RD S1 (unique items)
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 2/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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12458362   BIOSIS NO.: 200000211864
Pharmacokinetics of 111In- and 125I-labeled antiTac single-chain Fv
  recombinant immunotoxin.
AUTHOR: Kobayashi Hisataka; Kao Chih-Hao K; Kreitman Robert J; Le Nhat; Kim
  Meyoung-Kon; Brechbiel Martin W; Paik Chang H; Pastan Ira; Carrasquillo
  Jorge A(a)
AUTHOR ADDRESS: (a)Department of Nuclear Medicine, National Institutes of
  Health, 10 Center Dr., Bldg. 10, Rm. 1C496, Bethesda, MD, 20892-1180**USA
JOURNAL: Journal of Nuclear Medicine  41 (4):p755-762 April, 2000
ISSN: 0161-5505
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The use of immunotoxins for cancer therapy is an attractive
  strategy that exploits the targeting specificity of monoclonal
  antibodies and their fragments as well as the exquisite toxicity of
  the toxins. However, few studies of immunotoxins have evaluated their
  biodistribution in vivo. Previous studies have used 125I for tracing
  immunotoxin biodistribution in mice. Because the immunotoxin works only
  when it is internalized and because of known problems with quick
  dehalogenation after internalization of antibodies, we decided to
  use 111In, which has greater intracellular retention than iodine.
  Methods: To trace the in vivo pharmacokinetics of the immunotoxin in
  mice, we labeled the antiTac(Fv)-PE38 with 111In and compared it with
  125I-labeled antiTac(Fv)-PE38. We successfully labeled antiTac(Fv)-PE38
  with 111In at up to 2.96 GBq/mg. A 3- to 4-fold decrease in
  cytotoxicity was observed for both radiolabeled preparations. We
  evaluated the internalization of 111In- and 125I-labeled antiTac(Fv)-PE38
  into ATAC4 cells (Tac-positive) as well as their biodistribution
```

and pharmacokinetics in vivo in mice. In addition, some mice receiving these reagents were co-infused with 30 **mg** L-lysine to inhibit renal accumulation. Results: Significantly more 111In- than 125I-labeled antiTac(Fv)-PE38 accumulated in the ATAC4 cells (20% versus 5% of initial surface-bound radioactivity; P < 0.001). In vivo, significantly more 111In- than 125I-labeled antiTac(Fv)-PE38 accumulated in the kidney (119 versus 31 percentage injected dose per gram (%ID/g); P < 0.001). The tumor accumulation of 111In-labeled antiTac(Fv)-PE38 at 96 h was 13-fold greater than that of 125I-labeled antiTac(Fv)-PE38 (1.4 versus 0.1 %ID/g; P < 0.001). No antiTac(Fv)-PE38 was excreted into the urine in its intact form unless lysine was co-infused. Co-injected lysine reduced the renal accumulation of 111In-labeled antiTac(Fv)-PE38 by 62%. Conclusion: We evaluated the biodistribution, pharmacokinetics, and catabolism of 111In-labeled antiTac(Fv)-PE38 and found that it differed from 125I-labeled antiTac(Fv)-PE38. These studies suggest that 111In-labeled antiTac(Fv)-PE38 can be used to trace the fate of antiTac(Fv)-PE38 in humans.

2/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08785022 BIOSIS NO.: 199395074373
Prolongation of graft survival in primate allograft transplantation by yttrium-90-labeled anti-Tac in conjunction with granulocyte colony-stimulating factor.
AUTHOR: Parenteau Gary L; Dirbas Frederick M; Garmestani Kayhan; Brechbiel Martin W; Bukowski Maria A; Goldman Carolyn K; Clark Richard; Gansow Otto A; Waldmann Thomas A(a)
AUTHOR ADDRESS: (a)Metabolism Branch, National Cancer Inst., Bldg. 10, Room 4N115, National Inst. Health, Bethesda,
JOURNAL: Transplantation (Baltimore) 54 (6):p963-968 1992
ISSN: 0041-1337
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: High-affinity IL-2 receptors are expressed by T cells activated in response to foreign histocompatibility antigens but not by normal resting T cells. To exploit this difference in IL-2R expression, anti-**Tac**, a murine monoclonal **antibody** specific for the IL-2R-alpha subunit, was used to inhibit organ allograft rejection. To enhance its effector function, anti-**Tac** was armed by chelation with **yttrium**-90, a pure beta-emitting radionuclide. Animals received no immunosuppression (n=5, group I, controls), unmodified anti-**Tac** (n=5, 1 **mg**/kg, q.o.d., group II), or **90Y**-anti-**tac** (n=5, 1.6 mCi/kg divided into four doses, group III). The animals in group IV (n=4) were treated identically to those in group III with the exception that 5 mu-g/kg/dose of granulocyte colony-stimulating factor was administered intramuscularly on the days when the **yttrium**-90 was given and on postoperative days 12 through 35 in order to reduce hematopoietic toxicity. Mean graft survival +- S.E.M. for the control group was 8.2+-0.5 days as compared with 13.8+-2.1 days (P lt 0.05) for those monkeys treated with unmodified anti-**Tac**. Graft survival was further prolonged in animals of group III that received **90Y**-anti-**Tac**, with a mean graft survival of 45.0+-11.8 days; however, three of the five monkeys retained viable grafts within this group but died secondary to bone marrow suppression. In comparison, the monkeys in group IV that were treated with G-CSF in combination with **90Y**-anti-**Tac** had a mean graft survival of 49.2+-2.9 days. In contrast to group III there were no deaths in the group (IV) receiving G-CSF. Furthermore, animals in group IV had a reduced magnitude and shortened duration of irradiation-induced neutropenia when compared with that observed in group III animals that did not receive G-CSF. Thus, treatment with **90Y**-anti-**tac** in conjunction with G-CSF may have

102022586 CA: 102(3)22586x JOURNAL
Expression of interleukin 2 receptors on activated human B cells
AUTHOR(S): Waldmann, Thomas A.; Goldman, Carolyn K.; Robb, Richard J.; Depper, Joel M.; Leonard, Warren J.; Sharrow, Susan O.; Bongiovanni, Kathleen F.; Korsmeyer, Stanley J.; Greene, Warner C.
LOCATION: Metab. Branch, Natl. Cancer Inst., Bethesda, MD, 20205, USA
JOURNAL: J. Exp. Med. DATE: 1984 VOLUME: 160 NUMBER: 5 PAGES: 1450-66
CODEN: JEMEAV ISSN: 0022-1007 LANGUAGE: English

8/3/22 (Item 22 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

101205721 CA: 101(23)205721m JOURNAL
Pseudomonas exotoxin-anti-TAC. Cell-specific immunotoxin active against cells expressing the human T-cell growth factor receptor
AUTHOR(S): FitzGerald, David J. P.; Waldmann, Thomas A.; Willingham, Mark C.; Pastan, Ira
LOCATION: Lab. Mol. Biol., Natl. Cancer Inst., Bethesda, MD, 20205, USA
JOURNAL: J. Clin. Invest. DATE: 1984 VOLUME: 74 NUMBER: 3 PAGES: 966-71 CODEN: JCINAO ISSN: 0021-9738 LANGUAGE: English

8/3/23 (Item 23 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

101105569 CA: 101(13)105569z JOURNAL
Phorbol diester induces expression of Tac antigen on human acute T lymphocytic leukemic cells
AUTHOR(S): Greene, Warner C.; Robb, Richard J.; Depper, Joel M.; Leonard, Warren J.; Drogula, Cynthia; Svetlik, Penny B.; Wong-Staal, Flossie; Gallo, Robert C.; Waldmann, Thomas A.
LOCATION: Lab. Tumor Cell Biol., Natl. Cancer Inst., Bethesda, MD, USA
JOURNAL: J. Immunol. DATE: 1984 VOLUME: 133 NUMBER: 2 PAGES: 1042-7
CODEN: JOIMA3 ISSN: 0022-1767 LANGUAGE: English

8/3/24 (Item 24 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

100083564 CA: 100(11)83564u JOURNAL
Hairy cell leukemia: a malignant expansion of B cells which express Tac antigen
AUTHOR(S): Greene, Warner C.; Waldmann, Thomas A.; Cossman, Jeffrey; Hsu, Su Ming; Neckers, Leonard M.; Marshall, Sandra L.; Jensen, Jane P.; Bakhshi, Ajay; Leonard, Warren J.; et al.
LOCATION: Metab. Branch, Natl. Cancer Inst., Bethesda, MD, 20205, USA
JOURNAL: UCLA Symp. Mol. Cell. Biol., New Ser. DATE: 1983 VOLUME: 9
NUMBER: Norm. Neoplast. Hematopoiesis PAGES: 501-11 CODEN: USMBD6
LANGUAGE: English

8/3/25 (Item 25 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

100004419 CA: 100(1)4419z CONFERENCE PROCEEDING
Monoclonal anti-Tac blocks the action and membrane binding of human interleukin-2
AUTHOR(S): Depper, Joel M.; Leonard, Warren J.; Smith, Kendall A.; Waldmann, Thomas A.; Greene, Warner C.

LOCATION: Metab. Branch, Natl. Cancer Inst., Bethesda, MD, USA
JOURNAL: Interleukins, Lymphokines, Cytokines, Proc. Int. Lymphokine Workshop, 3rd EDITOR: Oppenheim, Joost J. (Ed), Cohen, Stanley (Ed), Landy, Maurice (Ed), DATE: 1983 PAGES: 19-26 CODEN: 50OPAC LANGUAGE: English MEETING DATE: 820000 PUBLISHER: Academic,New York, N. Y

8/3/26 (Item 26 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

99086331 CA: 99(11)86331n JOURNAL
Blockade of the interleukin-2 receptor by anti-Tac antibody: inhibition of human lymphocyte activation
AUTHOR(S): Depper, Joel M.; Leonard, Warren J.; Robb, Richard J.; Waldmann, Thomas A.; Greene, Warner C.
LOCATION: Metab. Branch, Natl. Cancer Inst., Bethesda, MD, 20205, USA
JOURNAL: J. Immunol. DATE: 1983 VOLUME: 131 NUMBER: 2 PAGES: 690-6
CODEN: JOIMA3 ISSN: 0022-1767 LANGUAGE: English

s3/k/1,21,47,50,54,62,68,70,71

3/K/1 (Item 1 from file: 653)
DIALOG(R)File 653:(c) format only 2000 The Dialog Corp. All rts. reserv.

... specific for tumor cells. With the possible exception of the antigens associated with B-cell **lymphoma** against which anti-idiotype antibodies are directed, no tumor-specific antigens suitable as targets for ...
... possible exceptions are anti-idiotype antibodies, but any such antibody is specific for the B-**lymphoma** cells of only one individual, and thus must be separately developed and isolated for each...e.g., cancer cells) in vivo have been developed. Examples of such MAbs are anti-**TAC**, or other interleukin-2 receptor **antibodies**; 9.2.27 and NR-ML-05 to a 250 kilodalton human melanoma associated proteoglycan...flow of inert gas.

The chelate is then conjugated to a Fab fragment of monoclonal **antibody** TFS-2 and a Fab fragment of TFS-4 in separate reaction mixtures. The Fab fragments are generated by papain **treatment** according to conventional procedures.

A buffered solution of the **antibody** fragment (5 **mg**/mL, 0.5 mL) is added to the purified sup 188 Re-labeled chelate, followed...

3/K/21 (Item 19 from file: 654)
DIALOG(R)File 654:(c) format only 2000 The Dialog Corp. All rts. reserv.

... AIDS, Meningitis, Arthritis) and therapy of tumors expressing IL-2 receptor such as T-cell **leukemia**.

In fact, the administration of B-B10 on the graft-versus-host reaction as produced... present some other examples in addition to those as hereinabove mentioned. For instance, an anti-**Tac antibody** is humanized by transplantation of nine amino acid residues on the framework in addition to ...
...activated human T cell as illustrated in Examples 11 and 14.

The humanized B-B10 **antibody** of the invention is parenterally **administered** with a dosage of about 0.05-500 **mg** for **treatment** and prevention of diseases caused by graft-versus-host reaction or host-versus-graft reaction...

... AIDS, meningitis, arthritis), and therapy of tumors expressing IL-2 receptor such as T-cell **leukemia**.

ADVANTAGEOUS EFFECT OF THE INVENTION

1) Half-life of mouse Mab in blood is about...

3/K/47 (Item 45 from file: 654)
DIALOG(R)File 654:(c) format only 2000 The Dialog Corp. All rts. reserv.

OTHER REFERENCES

...Statton, New York, pp. 283-301 (1986).

Hale et al., "Remission Induction in Non-Hodgkin **Lymphoma** with

Reshaped Human Monoclonal Antibody CAMPATH-1H," Lancet, Dec. 17, 1988, pp. 1394-1399.

Hieter...virus infection in vivo," Bio/Technology, 9:26-271 (1991).

Uchiyama et al., "A monoclonal **antibody** (anti-**Tac**) reactive with activated and functionally mature human T-cells," J. Immunol., 126:1393-1397 (1981...

...heavy chain (B) (SEQ ID NOS:3 and 4) variable regions of the mouse anti-**Tac** **antibody** (upper lines), compared with the human Eu **antibody** (lower lines), not including signal sequences. The three CDR's in each chain are underlined... FIG. 7A through FIG. 7D. Fluorocytometry of HUT-102 and Jurkat cells stained with anti-**Tac** **antibody** or humanized anti-**Tac** **antibody** followed respectively by fluorescein-conjugated goat anti-mouse Ig **antibody** or goat anti-human Ig antibody, as labeled. In each panel, the dotted curve shows...

... then with phycoerythrin-conjugated avidin. (B) Fluorocytometry of HUT-102 cells stained with the indicated **antibody** , then with biotinylated anti-**Tac**, and then with phycoerythrin-conjugated avidin.

FIG. 9A and FIG. 9B. Schematic diagram of the...NOS:7 and 8) chain variable regions of the PDL and CDR-only humanized anti-**Tac** **antibodies**. The PDL sequence is shown on the upper line, the CDR-only sequence below. Amino...

... light (B) (SEQ ID NO:10) chain variable regions of the CDR-only humanized anti-**Tac** **antibody** including signal sequences. Oligonucleotides used for gene synthesis are marked by solid lines: above, for...

... 12. FACS analysis of HUT-102 cells stained with PDL and CDR-only humanized anti-**Tac** **antibodies** and negative control **antibody** Fd79.

FIG. 13. Competition by mouse, PDL humanized, and CDR-only humanized anti-**Tac** **antibodies** with binding of radioiodinated mouse anti-**Tac** **antibody** to HUT-102 cells.

FIG. 14. Scheme for anchored polymerase chain reaction (PCR) cloning of ...IL-2 stimulated proliferation of human PHA blasts by humanized mik-beta 1+humanized anti-**Tac** **antibodies**. No **antibody** added (quadrature), 2 ug each of humanized mik- beta 1 and humanized anti-Tac added...
...human antibody (e.g., A.T.C.C. Accession No. CRL 9688 secretes an anti-**Tac** chimeric **antibody**), although other mammalian species may be used.

As used herein, the term "humanized" immunoglobulin refers...2 receptor's structure and function is due to the development of specifically reactive monoclonal **antibodies**. In particular, one mouse monoclonal **antibody**, known as anti-**Tac** (Uchiyama, et al., J. Immunol. 126, 1393 (1981)) has been used to show that IL...

...the IL-2 receptor (Herrmann, et al., J. Exp. Med. 162, 1111 (1985)).

The anti-**Tac** monoclonal **antibody** has also been used to define lymphocyte functions that require IL-2 interaction, and has...

... of cytotoxic and suppressor T lymphocytes in cell culture. Also, based on studies with anti-**Tac** and other **antibodies**, a variety of disorders are now associated with improper IL-2 receptor expression by T-cells, in particular adult T-cell **leukemia**.

More recently, the IL-2 receptor has been shown to be an ideal ... approaches to T-cell mediated diseases. It has been proposed that IL-2 receptor specific **antibodies**, such as the anti-**Tac** monoclonal **antibody** , can be used either alone or as an immunoconjugate (e.g., with Ricin A, isotopes...

... the IL-2 receptor. These agents can, for example, theoretically eliminate IL-2 receptor-expressing **leukemic** cells, certain B-cells, or activated T-cells involved in a disease state, yet allow...

... response by activated T-cells. Indeed, clinical trials have been initiated using, e.g., anti-**Tac** **antibodies** (see, generally, Waldmann, T., et al., Cancer Res. 45, 625 (1985), Waldmann, T., Science 232 herein by reference).

Unfortunately, the use of the anti-**Tac** and other non-human monoclonal **antibodies** have certain drawbacks, particularly in repeated therapeutic regimens as explained below. Mouse monoclonal antibodies, for...

... and lack other important immunoglobulin functional characteristics when used in humans.

Perhaps more importantly, anti-**Tac** and other non-human monoclonal **antibodies** contain substantial stretches of amino acid sequences that will be immunogenic when injected into a...binding to a desired epitope on the human IL-2 receptor, such as the anti-**Tac** monoclonal **antibody** . The DNA segments encoding these regions will typically be joined to DNA segments encoding appropriate...selected primarily based on fluid volumes, viscosities, etc., in accordance with the particular mode of **administration** selected.

Thus, a typical pharmaceutical composition for injection could be made up to contain 1 ml sterile buffered water, and 1 to 50 **mg** of **antibody** . A typical composition for intravenous infusion could be made up to contain 250 ml of sterile Ringer's solution, and 150 **mg** of **antibody**. Actual methods for preparing parenterally **administrable** compositions will be known or apparent to those skilled in the art and are described...

... 15th ed., Mack Publishing Company, Easton, Pa. (1980), which is incorporated herein by reference.

The **antibodies** of this invention can be frozen or lyophilized for storage and reconstituted in a suitable... the disease and its complications. An amount adequate to accomplish this is defined as a " **therapeutically** effective dose." Amounts effective for this use will depend upon the severity of the infection...

... the patient's own immune system, but generally range from about 1 to about 200 **mg** of **antibody** per dose, with dosages of from 5 to 25 mg being more commonly used. It...of health and general level of immunity, but generally range from 0.1 to 25 **mg** per dose, especially 0.5 to 2.5 **mg** per dose. A preferred prophylactic use is for the prevention of kidney transplant rejection.

Single or multiple **administrations** of the compositions can be carried out with dose levels and pattern being selected by the **treating** physician. In any event, the pharmaceutical formulations should provide a quantity of the **antibody**(ies) of this invention sufficient to effectively **treat** the patient.

Human-like **antibodies** of the present invention can further find a wide variety of utilities in vitro. By way of example, the **antibodies** can be utilized for T-cell typing, for isolating specific IL-2 receptor bearing cells... human-like antibody binding to p75 of the IL-2 receptor,

i.e., humanized anti-**Tac** plus humanized mik- beta 1.

Human-like **antibodies** of the present invention can further find a wide variety of utilities in vitro. By... cell type, such as cells expressing an HSV epitope.

The compositions containing the present humanized **antibodies** or a cocktail thereof can be **administered** for prophylactic and/or **therapeutic treatments**. In **therapeutic** application, compositions are **administered** to a patient already suffering from HSV infection, in an amount sufficient to cure or...

...the disease and its complications. An amount adequate to accomplish this is defined as a "**therapeutically** effective dose." Amounts effective for this use will depend upon the severity of the infection...

... the patient's own immune system, but generally range from about 1 to about 200 **mg** of **antibody** per dose, with dosages of from 5 to 25 **mg** being more commonly used. It must be kept in mind that the materials of this... humanized immunoglobulins of this invention, it is possible and may be felt desirable by the **treating** physician to **administer** substantial excesses of these **antibodies**.

In prophylactic applications, compositions containing the present immunoglobulins or a cocktail thereof are **administered** to a patient not already in a disease state to enhance the patient's resistance...

...of health and general level of immunity, but generally range from 0.1 to 25 **mg** per dose. A preferred prophylactic use is for the prevention of herpes in immunocompromised patients, such as organ transplant recipients.

Single or multiple **administrations** of the compositions can be carried out with dose levels and pattern being selected by the **treating** physician. In any event, the pharmaceutical formulations should provide a quantity of the **antibody**(ies) of this invention sufficient to effectively **treat** the patient.

Humanized **antibodies** of the present invention can further find a wide variety of utilities in vitro. By way of example, the **antibodies** can be utilized for detection ...about 10,000-15,000 new cases of myeloid (also called non-lymphocytic or granulocytic) **leukemia** in the U.S. per year (Cancer Facts & Figures, American Cancer Society, 1987). There are two major forms of myeloid **leukemia**: acute myelogenous **leukemia** (AML) and chronic myelogenous **leukemia** (CML). Despite treatment with chemotherapy, long-term survival in patients with AML is less than... ... Hematology 4, 221 (1986)), and survival with CML and related diseases such as chronic myelomonocytic **leukemia** (CMML), chronic monocytic **leukemia** (CMMOL) and myelodysplastic syndrome (MDS) is even lower.

The p67 protein or CD33 antigen is found on the surface of progenitors of myeloid cells and of the **leukemic** cells of most cases of AML, but not on lymphoid cells or non-hematopoietic cells124 (1983) and Griffin et al., **Leukemia** Research 8, 521 (1984), both of which are incorporated herein by reference).

Another antibody that binds to CD33 is M195 (Tanimoto et al., **Leukemia** 3, 339 (1989) and Scheinberg et al., **Leukemia** 3, 440 (1989), both of which are incorporated herein by reference). The reactivity of M195...

... 9, 207 (1990)). M195 radiolabeled with iodine-131 was found to rapidly and specifically target **leukemic** cells in both the blood and bone marrow.

Unfortunately, the use of non-human monoclonal...needs.

The present invention provides novel compositions useful, for example, in

the treatment of myeloid **leukemia** -related human disorders, the compositions containing humanized immunoglobulins specifically capable of binding to CD33 antigen...form, or together with a chemotherapeutic agent such as cytosine arabinoside or daunorubicin active against **leukemia** cells, or complexed with a radionuclide such as iodine-131. All of these compounds will be particularly useful in treating **leukemia** and myeloid cell-mediated disorders. The humanized immunoglobulins or their complexes can be prepared in...

...to 10 sup 10 M sup -1 or stronger, are capable of, e.g., destroying **leukemia** cells. The humanized immunoglobulins will have a human framework and will have one or ...additional agents (e.g., 6-thioguanine) well-known to those skilled in the art for **leukemia** treatment may also be utilized (see, Hoffbrund & Pettit., op. cit.).

A preferred pharmaceutical composition of the present invention comprises the use of the subject immunoglobulins in immunotoxins to kill **leukemia** cells. ...examples are offered by way of illustration, not by limitation.

EXPERIMENTAL

Example 1

Humanized anti-**Tac Antibody**

Design of Genes for Humanized anti-**Tac** Light and Heavy Chains

The sequence of the human **antibody** Eu (Sequences of Proteins of Immunological Interest, E. Kabat et al., U.S. Dept. of...

... humanized antibody, because the amino acid sequence of the heavy chain variable region of anti-**Tac** is more homologous to the heavy chain of this **antibody** than to any other complete heavy chain variable region sequence in the National Biomedical Foundation...heavy chain (amino acids 30 and 67); or

(4) 3-dimensional modeling of the anti-**Tac antibody** suggested that the amino acid was physically close to the antigen binding region (amino acids...do not express the IL-2 receptor (FIG. 7D). As controls, the original mouse anti-**Tac antibody** was also used to stain these cells, giving similar results.

For the next experiments, cells...Laboratories, Inc., Richmond, Calif.) according to standard techniques. To determine the affinity of the humanized **antibody** relative to the original anti-**Tac antibody** , a competitive binding experiment was performed. About 5X10 sup 5 HUT-102 cells were incubated with known quantities (10-40 ng) of the anti-**Tac antibody** and the humanized anti-**Tac antibody** for 10 min at 4 degree(s) C. Then 100 ng of biotinylated anti-Tac of increasing amounts (10-40 ng) of the anti-**Tac antibody** as competitor in the first step decreased the amount of biotinylated anti-Tac that could...

...with the biotinylated anti-Tac, thus decreasing fluorescence more.

Example 2

A Second Humanized anti-**Tac Antibody**

Higher Level Expression of the Humanized anti-**Tac Antibody**

Three new plasmid vectors were prepared for expression of the humanized antibodies. The plasmid pVg1...Xba I sites of the plasmid vectors pVk and pVg1. To express the humanized anti-**Tac antibody**, the light chain encoding plasmid was introduced by electroporation into SP2/0 mouse

myeloma cells...

...supernatant of transfected cells by protein A sepharose chromatography.

Construction of the Second Humanized anti-**Tac Antibody**

To determine whether it was actually necessary to use the mouse anti- Tac amino acids in categories (2)-(4) in the humanized anti-**Tac antibody** to retain binding affinity, a second humanized anti-**Tac antibody** was constructed. In the second **antibody**, only mouse anti-**Tac** amino acids in Category (1), i.e., in the CDR's themselves, were used, with...

...coming from the human Eu framework. For purposes of this discussion, the original humanized anti-**Tac antibody** will be called the "PDL humanized **antibody**," and the second humanized antibody will be called the "CDR-only humanized antibody." The amino...detectably bind the IL-2 receptor.

Binding of the PDL and CDR-only humanized anti-**Tac antibodies** to the IL-2 receptor were also compared in a competitive binding assay. Approximately 4X10 sup 5 HUT-102 cells were incubated with 1.5 ng of radioiodinated mouse anti-**Tac antibody** (7X10 sup 6 cpm/ug) and varying amounts of each humanized antibody (4 to 512...were collected by centrifugation and radioactivity was measured. The relative binding by the two humanized **antibodies** and by mouse anti-**Tac** is shown in a plot of bound/free labelled **antibody** versus competitor concentration (FIG. 13). The PDL humanized anti-**Tac antibody** affinity for IL-2 receptor is essentially equal to that of the mouse anti-**Tac antibody** , because it competes about equally well. But competition by the CDR-only humanized anti-**Tac antibody** to IL-2 receptor was undetectable at the **antibody** concentrations used, indicating a binding affinity reduction of at least 100-fold as compared to the PDL humanized anti-**Tac antibody**. Because the sequences of the PDL and CDR humanized anti-**Tac antibodies** differ only at positions where mouse framework residues in categories (2)-(4) were used in...of herpes simplex virus (Metcalf et al., Intervirology 29, 39 (1988)), M195 (Tanimoto et al., **Leukemia** 3, 339 (1989)) which binds to the CD33 antigen, mik- beta 1 (Tusdo et al...of the humanized antibody, because the amino acid sequence of the heavy chain of anti-**Tac** is more homologous to the heavy chain of this **antibody** than to any other heavy chain sequence in the National Biomedical Foundation Protein Identification Resourceamino acids 30 and 67).

(4) 3-dimensional modeling of the anti-**Tac antibody** suggested that the amino acid was physically close to the antigen binding region (amino acids...do not express the IL-2 receptor (FIG. 7D). As controls, the original mouse anti-**Tac antibody** was also used to stain these cells (FIG. 7B and FIG. 7C), giving similar resultsTo determine the affinity of the humanized **antibody** relative to the original anti-**Tac antibody** , a competitive binding experiment was performed. About 5X10 sup 5 HUT-102 cells were incubated with known quantities (10-40 ng) of the anti-**Tac antibody** and the humanized anti-**Tac antibody** for 10 min at 4 degree(s) C. Then 100 ng of biotinylated anti-Tac...

...fluorescence on a FACSCAN cytofluorometer.

Use of increasing amounts (10-40 ng) of the anti-**Tac antibody** as competitor in the first step decreased the amount of biotinylated anti- ... if one had greater affinity, it would have more effectively competed with the biotinylated anti-**Tac**, thus decreasing fluorescence more.

Biological Properties of the Humanized **Antibody**

For optimal use in treatment of human disease, the humanized antibody should be able to...

...cell such as a macrophage that can lyse the target. To determine whether the humanized **antibody** and the original mouse anti-**Tac** **antibody** can mediate ADCC, a chromium release assay was performed by standard methods. Specifically, human **leukemia** HUT-102 cells, which express the IL-2 receptor, were incubated with sup 51 Cr...

... this radionuclide. The HUT-102 cells were then incubated with an excess of either anti-**Tac** or humanized anti-**Tac** **antibody**. The HUT-102 cells were next incubated for 4 hrs with either a 30:1...

... is likely to be more efficacious than the original mouse antibody in treating T-cell **leukemia** or other T-cell mediated diseases.

TABLE 3Higher Level Expression of the Humanized anti-**Tac Antibody**

Two new plasmid vectors were prepared for expression of the humanized antibody. The plasmid pVg1... Xba I sites of the plasmid vectors pVk and pVG1. To express the humanized anti-**Tac** **antibody**, the light chain encoding plasmid was introduced by electroporation into SP2/0 mouse myeloma cells...

... immunoglobulins of the present invention offer numerous advantages of other human IL-2 receptor-specific **antibodies**. In comparison to anti-**Tac** mouse monoclonal **antibodies** , the present human-like immunoglobulin can be more economically produced and contain substantially less foreign... antibody was within about 2-fold of the affinity of the mouse mik- beta 1 **antibody**.

The ability of humanized mik- beta 1 plus humanized anti-**Tac** **antibody** to inhibit IL-2 stimulated proliferation of human lymphocytes was determined. Human mononuclear cells, collected...of the antibodies will have strong immunosuppressive properties. Humanized mik-beta 1 plus humanized anti-**Tac** inhibited proliferation much more strongly than did either **antibody** alone.

From the foregoing, it will be appreciated that the humanized immunoglobulins of the present...
...First and second polynucleotides according to claim 1, wherein the donor immunoglobulin is the anti-**Tac** **antibody** or the M195 **antibody**.

5. First and second polynucleotides according to claim 1 wherein the acceptor immunoglobulin heavy and... second polynucleotides according to claim 10 or 11, wherein the donor immunoglobulin is the anti-**Tac** **antibody** or the M195 **antibody**.

15. A vector comprising first and second polynucleotides according to claim 10.

16. A vector...

3/K/50 (Item 48 from file: 654)
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...for dividing cells.

Chemotherapy for cancer has improved survival in some cancers such as childhood **leukemia** but the survival rate for advanced (metastatic) solid tumors has not dramatically increased in over...cell division. (Cancer, Edited by V. T. Devita et al. 1985 p50 supra).

A monoclonal **antibody** **Tac** has been reported (Uchiyama et al. J. Immunol. 1981, 126 1393-1397). It appears to...

... interleukin 2 receptor present on activated T lymphocytes but not present on the majority of **leukemia** cells. However CBL1 has a different antigenic specificity to the **Tac antibody**. CBL1 reacts with **leukemia** cell lines but **Tac** does not. The molecular weight of the CBL1 antigenic determinant is 15,000 daltons. This... antibodies will also find use in detection of malignant cells and in immunological classification of **leukemia**. **Leukemias** can be divided into immunological subsets depending on the particular surface antigens displayed by the...

... CBL1 antibody is reactive with three out of the four generally recognised morphological types of **leukemia**, being nonreactive with chronic lymphocytic **leukemia** (CLL). CBL1 would thus be useful, in combination with other antibodies having different specificities, in clinical diagnosis of a patient having **leukemia**. Malignant lymphocyte cells which are incapable of reacting with CBL1 would be presumed to be... old female Balb/c mice (Simonsen Labs) were immunised intravenously with 2X10 sup 6 acute **leukemia** cells weekly for 3 weeks. Three days after the final injection the spleens were removed...by exclusion gel filtration on S300 (Sephadex sup R). Materials used in characterisation of CBL1.

Leukemia Cells:

Heparinised peripheral blood samples were drawn from children and adults with active **leukemia**. The acute lymphocytic **leukemia** (ALL,) end acute myelocytic **leukemia** (AML) patients had peripheral blood blast counts greater than 90%. **Leukemia** cells from patients and peripheral blood lymphocytes from healthy donors were isolated by Ficoll-Hypaque sup R density gradient centrifugation. **Leukemia** cells were stored in liquid nitrogen.

Cell lines were grown in suspension cultures in RPMI...
... of human cell types. The cells that were highly positive were cultured solid tumor cells, **leukemia** cells, activated lymphocytes and monocytes. Most normal non-dividing tissue cells were not reactive. Therefore...blood monocutes

	15	>80%
Peripheral blood activated		
	6	>60%
lymphocytes		
Malignant cells - Type		
Acute myeloid **leukemias**		
	25	>95%
Acute lymphoid **leukemias**		
	28	>95%
Chronic myeloid blast crisis		
	10	>95%
Chronic lymphocytic **leukemias**		
	20	<2%
Cultured **leukemia** cell lines,		
	10	>95%
Reh, CEM, HSB2, Daudi,		
Raji, HL60, KG, JM, Molt 4,		
BJABE. Human Studies		

Nineteen patients with severe steroid resistant kidney graft rejections were **treated** with the monoclonal **antibody**. Five **mg** in 200 ml of saline ...was given intravenously on 9 successive days. None of the 19 patients developed fever, vomiting, **treatment** created infections or other side effects. All patients had previously been immunosuppressed with conventional antirejection...abdomen causing a large tumor abscess on the left groin and protruding rectal tumor was **treated** with CBL1 purified monoclonal **antibody**. Following ten daily **treatments** of 20 **mg** per day the tumor abscess healed completely and the protruding rectal tumor receded.

Case 4...

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... therapy is further discussed in the two articles; Kozak et al, "Bismuth-212-labeled anti-**Tac** monoclonal **antibody** : Alpha-particle-emitting Radionuclides ... diseases, cardiovascular diseases, inflammatory conditions and other pathological conditions.

The cancer states include carcinomas, sarcomas, **leukemias**, **lymphomas**, myelomas and neural tumors.

The infectious diseases include those caused by invading microbes or parasites...Respiratory syncytial virus
Varicella-Zoster virus
Hepatitis B virus
Measles virus
Adenovirus
Human T-cell **leukemia** viruses
Epstein-Barr virus
Murine **leukemia** virus*
Mumps virus
Vesicular stomatitis virus
Sindbis virus
Lymphocytic choriomeningitis virus
Wart virus
Blue tongue virus
Sendai virus
Feline **leukemia** virus*
Reo virus
Polio virus
Simian virus 40*
Mouse mammary tumor virus*
Dengue virus
Rubella...

... antibody fragments reactive with a tumor associated antigens present on carcinoma or sarcoma cells or **lymphomas** . Such antibodies are disclosed, e.g., in Goldenberg et al., Journal of Clinical Oncology, Vol... in vivo with a wide variety of other radiometals of use in cancer detection and **therapy**. Thus, a patient could be imaged with the In-111 **antibody** conjugate of the ligand and thereafter **treated** with the yttrium complex of the same **antibody** chelate conjugate, thus facilitating calculation of the dose of radioactivity transported to the patient's tumor and so increasing likelihood of the effective application of the **therapy**.

The metal chelate conjugated **antibodies** of this invention can be **administered** in vivo in any suitable pharmaceutical carrier. As noted earlier, a physiologic normal saline solution...

...include a minor amount of carrier protein such as human serum albumin to stabilize the **antibody**. The concentration of metal chelate ... conjugated antibodies within the solution will be a matter of choice. Levels of 0.5 **mg** per ml are readily attainable but the concentrations may vary considerably depending upon the specifics...

... addition to these located at the site, the circulating antigens can be removed prior to **treatment** . Such removal of antigens can be accomplished, of example, by the use of unlabeled **antibodies**, or by plasmapheresis in which the patient's serum is **treated** to removed antigens.

A physiological solution of the protein conjugate is advantageously

metered into sterile metal free vials, e.g., at a unit dosage of about 0.1-100 **mg** protein conjugate/vial, and the vials are either stoppered, sealed and stored at low temperature...
... claim 1, wherein said antibody or antibody fragment specifically binds to an antigen associated with **lymphomas**, carcinomas, sarcomas, **leukemias**, myelomas or neural tumors.

4. The conjugate of claim 1, wherein said marker is a...

... antibody or F(ab') sub 2 antibody fragment specifically binds to an antigen associated with **lymphomas**, carcinomas, sarcomas, **leukemias**, myelomas or neural tumors.

16. A method for preparing a precursor conjugate of a therapeutic...

3/K/62 (Item 60 from file: 654)
DIALOG(R)File 654:(c) format only 2000 The Dialog Corp. All rts. reserv.

OTHER REFERENCES

...a mouse", Nature 321:522-525 (1986).

Hale et al., "Remission Induction in Non-Hodgkin **Lymphoma** with Reshaped Human Monoclonal Antibody CAMPATH-1H", Lancet Dec. 17, 1988, pp. 1394-1399.

Chothia...

...heavy chain (B) [SEQ ID NOS:3 and 4] variable regions of the mouse anti-**Tac antibody** (upper lines), compared with the human Eu **antibody** (lower lines), not including signal sequences. The three CDR's in each chain are underlined...

... FIG. 7A through FIG. 7D. Fluorocytometry of HUT-102 and Jurkat cells stained with anti-**Tac antibody** or humanized anti-**Tac antibody** followed respectively by fluorescein-conjugated goat anti-mouse Ig **antibody** or goat anti-human Ig antibody, as labeled. In each panel, the dotted curve shows...

... then with phycoerythrin-conjugated avidin. (B) Fluorocytometry of HUT-102 cells stained with the indicated **antibody** , then with biotinylated anti-**Tac**, and then with phycoerythrin-conjugated avidin.

FIG. ... NOS:7 and 8] chain variable regions of the PDL and CDR-only humanized anti-**Tac antibodies**. The PDL sequence is shown on the upper line, the CDR-only sequence below. Amino...

... light (B) [SEQ ID NO:10] chain variable regions of the CDR-only humanized anti-**Tac antibody** including signal sequences. Oligonucleotides used for gene synthesis are marked by solid lines: above, for...

... 12. FACS analysis of HUT-102 cells stained with PDL and CDR-only humanized anti-**Tac antibodies** and negative control **antibody** Fd79.

FIG. 13. Competition by mouse, PDL humanized, and CDR-only humanized anti-**Tac antibodies** with binding of radioiodinated mouse anti-**Tac antibody** to HUT-102 cells.

FIG. 14. Scheme for anchored polymerase chain reaction (PCR) cloning of ...IL-2 stimulated proliferation of human PHA blasts by humanized mik- beta 1+humanized anti-**Tac antibodies**. No **antibody** added (quadrature), 2 ug each of humanized mik- beta 1 and humanized anti-Tac added...

...human antibody (e.g., A.T.C.C. Accession No. CRL 9688 secretes an anti-**Tac** chimeric **antibody**), although other mammalian species may be used.

As used herein, the term "humanized" immunoglobulin refers...2 receptor's structure and function is due to the development of specifically reactive monoclonal **antibodies**. In particular, one mouse monoclonal **antibody**, known as anti-**Tac** (Uchiyama, et al., J. Immunol. 126, 1393 (1981)) has been used to show that IL...

...the IL-2 receptor (Herrmann, et al., J. Exp. Med. 162, 1111 (1985)).

The anti-**Tac** monoclonal **antibody** has also been used to define lymphocyte functions that require IL-2 interaction, and has...

... of cytotoxic and suppressor T lymphocytes in cell culture. Also, based on studies with anti-**Tac** and other **antibodies**, a variety of disorders are now associated with improper IL-2 receptor expression by T-cells, in particular adult T-cell **leukemia**.

More recently, the IL-2 receptor has been shown to be an ideal target for ...
... approaches to T-cell mediated diseases. It has been proposed that IL-2 receptor specific **antibodies**, such as the anti-**Tac** monoclonal **antibody** , can be used either alone or as an immunoconjugate (e.g., with Ricin A, isotopes...

... the IL-2 receptor. These agents can, for example, theoretically eliminate IL-2 receptor-expressing **leukemic** cells, certain B-cells, or activated T-cells involved in a disease state, yet allow...

... response by activated T-cells. Indeed, clinical trials have been initiated using, e.g., anti-**Tac** **antibodies** (see, generally, Waldmann, T., et al., Cancer Res. 45, 625 (1985), Waldmann, T., Science 232 ...

...1989), all of which are incorporated herein by reference).

Unfortunately, the use of the anti-**Tac** and other non-human monoclonal **antibodies** have certain drawbacks, particularly in repeated therapeutic regimens as explained below. Mouse monoclonal antibodies, for...

... and lack other important immunoglobulin functional characteristics when used in humans.

Perhaps more importantly, anti-**Tac** and other non-human monoclonal **antibodies** contain substantial stretches of amino acid sequences that will be immunogenic when injected into a...binding to a desired epitope on the human IL-2 receptor, such as the anti-**Tac** monoclonal **antibody** . The DNA segments encoding these regions will typically be joined to DNA segments encoding appropriate...selected primarily based on fluid volumes, viscosities, etc., in accordance with the particular mode of **administration** selected.

Thus, a typical pharmaceutical composition for injection could be made up to contain 1 ml sterile buffered water, and 1 to 50 **mg** of **antibody** . A typical composition for intravenous infusion could be made up to contain 250 ml of sterile Ringer's solution, and 150 **mg** of **antibody**. Actual methods for preparing parenterally **administrable** compositions will be known or apparent to those skilled in the art and are described...

... 15th ed., Mack Publishing Company, Easton, Pa. (1980), which is incorporated herein by reference.

The **antibodies** of this invention can be frozen or lyophilized for

storage and reconstituted in a suitable...

...the disease and its complications. An amount adequate to accomplish this is defined as a "**therapeutically** effective dose." Amounts effective for this use will depend upon the severity of the infection...

... the patient's own immune system, but generally range from about 1 to about 200 **mg** of **antibody** per dose, with dosages of from 5 to 25 mg being more commonly used. It...

...of health and general level of immunity, but generally range from 0.1 to 25 **mg** per dose, especially 0.5 to 2.5 **mg** per dose. A preferred prophylactic use is for the prevention of kidney transplant rejection.

Single or multiple **administrations** of the compositions can be carried out with dose levels and pattern being selected by the **treating** physician. In any event, the pharmaceutical formulations should provide a quantity of the **antibody**(ies) of this invention sufficient to effectively **treat** the patient.

Human-like **antibodies** of the present invention can further find a wide variety of utilities in vitro. By way of example, the **antibodies** can be utilized for T-cell typing, for isolating specific IL-2 receptor bearing cells... human-like antibody binding to p75 of the IL-2 receptor, i.e., humanized anti-**Tac** plus humanized mik- beta 1.

Human-like **antibodies** of the present invention can further find a wide variety of utilities in vitro. By... cell type, such as cells expressing an HSV epitope.

The compositions containing the present humanized **antibodies** or a cocktail thereof can be **administered** for prophylactic and/or **therapeutic treatments**. In **therapeutic** application, compositions are **administered** to a patient already suffering from HSV infection, in an amount sufficient to cure or...

...the disease and its complications. An amount adequate to accomplish this is defined as a "**therapeutically** effective dose." Amounts effective for this use will depend upon the severity of the infection...

... the patient's own immune system, but generally range from about 1 to about 200 **mg** of **antibody** per dose, with dosages of from 5 to 25 **mg** being more commonly used. It must be kept in mind that the materials of this... humanized immunoglobulins of this invention, it is possible and may be felt desirable by the **treating** physician to **administer** substantial excesses of these **antibodies**.

In prophylactic applications, compositions containing the present immunoglobulins or a cocktail thereof are **administered** to a patient not already in a disease state to enhance the patient's resistance...

...of health and general level of immunity, but generally range from 0.1 to 25 **mg** per dose. A preferred prophylactic use is for the prevention of herpes in immunocompromised patients, such as organ transplant recipients.

Single or multiple **administrations** of the compositions can be carried out with dose levels and pattern being selected by the **treating** physician. In any event, the pharmaceutical formulations should provide a quantity of the **antibody**(ies) of this invention sufficient to effectively **treat** the patient.

Humanized **antibodies** of the present invention can further find a wide variety of utilities in vitro. By way of example, the **antibodies** can be utilized for detection of HSV antigens, for isolating specific HSV infected cells or...
...about 10,000-15,000 new cases of myeloid (also called non-lymphocytic or

granulocytic) **leukemia** in the U.S. per year (Cancer Facts & Figures, American Cancer Society, 1987). There are two major forms of myeloid **leukemia**: acute myelogenous **leukemia** (AML) and chronic myelogenous **leukemia** (CML). Despite treatment with chemotherapy, long-term survival in patients with AML is less than...

... Hematology 4, 221 (1986)), and survival with CML and related diseases such as chronic myelomonocytic **leukemia** (CMML), chronic monocytic **leukemia** (CMMOL) and myelodysplastic syndrome (MDS) is even lower.

The p67 protein or CD33 antigen is found on the surface of progenitors of myeloid cells and of the **leukemic** cells of most cases of AML, but not on lymphoid cells or non-hematopoietic cells...

... L4B3, L1B2 and MY9 (Andrews et al., Blood 62, 124 (1983) and Griffin et al., **Leukemia** Research 8, 521 (1984), both of which are incorporated herein by reference).

Another antibody that binds to CD33 is M195 (Tanimoto et al., **Leukemia** 3, 339 (1989) and Scheinberg et al., **Leukemia** 3, 440 (1989), both of which are incorporated herein by reference). The reactivity of M195...

... 9, 207 (1990)). M195 radiolabeled with iodine-131 was found to rapidly and specifically target **leukemic** cells in both the blood and bone marrow.

Unfortunately, the use of non-human monoclonal...

...needs.

The present invention provides novel compositions useful, for example, in the treatment of myeloid **leukemia** -related human disorders, the compositions containing humanized immunoglobulins specifically capable of ... form, or together with a chemotherapeutic agent such as cytosine arabinoside or daunorubicin active against **leukemia** cells, or complexed with a radionuclide such as iodine-131. All of these compounds will be particularly useful in treating **leukemia** and myeloid cell-mediated disorders. The humanized immunoglobulins or their complexes can be prepared in...

...to 10 sup 10 M sup -1 or stronger, are capable of, e.g., destroying **leukemia** cells. The humanized immunoglobulins will have a human framework and will have one or more...

... additional agents (e.g., 6-thioguanine) well-known to those skilled in the art for **leukemia** treatment may also be utilized (...of the present invention comprises the use of the subject immunoglobulins in immunotoxins to kill **leukemia** cells. Immunotoxins are characterized by two components and are particularly useful for killing selected cells... examples are offered by way of illustration, not by limitation.

EXPERIMENTAL

EXAMPLE 1

Humanized anti-**Tac antibody**

Design of genes for humanized anti-**Tac** light and heavy chains

The sequence of the human **antibody** Eu (Sequences of Proteins of Immunological Interest, E. Kabat et al., U.S. Dept. of...

... humanized antibody, because the amino acid sequence of the heavy chain variable region of anti-**Tac** is more homologous to the heavy chain of this **antibody** than to any other complete heavy chain variable region

sequence in the National Biomedical Foundation...heavy chain (amino acids 30 and 67); or

(4) 3-dimensional modeling of the anti-**Tac antibody** suggested that the amino acid was physically close to the antigen binding region (amino acids...do not express the IL-2 receptor (FIG. 7D). As controls, the original mouse anti-**Tac antibody** was also used to stain these cells, giving similar results.

For the next experiments, cells...

... Laboratories, Inc., Richmond, Calif.) according to standard techniques. To determine the affinity of the humanized **antibody** relative to the original anti-**Tac antibody** , a competitive binding experiment was performed. About 5X10 sup 5 HUT-102 cells were incubated with known quantities (10-40 ng) of the anti-**Tac antibody** and the humanized anti-**Tac antibody** for 10 min at 4 degree(s) C. Then 100 ng of biotinylated anti-Tac...

...fluorescence on a FACSCAN cytofluorometer.

Use of increasing amounts (10-40 ng) of the anti-**Tac antibody** as competitor in the first step decreased the amount of biotinylated anti-Tac that could... with the biotinylated anti-Tac, thus decreasing fluorescence more.

EXAMPLE 2

A second humanized anti-**Tac antibody**

Higher level expression of the humanized anti-**Tac antibody**

Three new plasmid vectors were prepared for expression of the humanized antibodies. The plasmid pVg1...

... Xba I sites of the plasmid vectors pVk and pVg1. To express the humanized anti-**Tac antibody**, the light chain encoding plasmid was introduced by electroporation into SP2/0 mouse myeloma cells...

...supernatant of transfected cells by protein A sepharose chromatography.

Construction of the second humanized anti-**Tac antibody**

To determine whether it was actually necessary to use the mouse anti-Tac amino acids in categories (2)-(4) in the humanized anti-**Tac antibody** to retain binding affinity, a second humanized anti-**Tac antibody** was constructed. In the second **antibody**, only mouse anti-**Tac** amino acids in Category (1), i.e., in the CDR's themselves, were used, with...

...coming from the human Eu framework. For purposes of this discussion, the original humanized anti-**Tac antibody** will be called the "PDL humanized **antibody**," and the second humanized antibody will be called the "CDR-only humanized antibody." The amino...detectably bind the IL-2 receptor.

Binding of the PDL and CDR-only humanized anti-**Tac antibodies** to the IL-2 receptor were also compared in a competitive binding assay. Approximately 4X10 sup 5 HUT-102 cells were incubated with 1.5 ng of radioiodinated mouse anti-**Tac antibody** (7X10 sup 6 cpm/ug) and varying amounts of each humanized antibody (4 to 512...

... were collected by centrifugation and radioactivity was measured. The relative binding by the two humanized **antibodies** and by mouse anti-**Tac** is shown in a plot of bound/free labelled **antibody** versus competitor concentration (FIG. 13). The PDL humanized anti-**Tac antibody** affinity for IL-2 receptor is essentially equal to that of

the mouse anti-**Tac antibody**, because it competes about equally well. But competition by the CDR-only humanized anti-**Tac antibody** to IL-2 receptor was undetectable at the **antibody** concentrations used, indicating a binding affinity reduction of at least 100-fold as compared to the PDL humanized anti-**Tac antibody**. Because the sequences of the PDL and CDR humanized anti-**Tac antibodies** differ only at positions where mouse framework residues in categories (2)-(4) were used in...

... of herpes simplex virus (Metcalf et al., Intervirology 29, 39 (1988)), M195 (Tanimoto et al., **Leukemia** 3, 339 (1989)) which binds to the CD33 antigen, mik- beta 1 (Tusdo et al...of the humanized antibody, because the amino acid sequence of the heavy chain of anti-**Tac** is more homologous to the heavy chain of this **antibody** than to any other heavy chain sequence in the National Biomedical Foundation Protein Identification Resource...

...Tac heavy chain (amino acids 30 and 67).
(4) 3-dimensional modeling of the anti-**Tac antibody** suggested that the amino acid was physically close to the antigen binding region (amino acids...do not express the IL-2 receptor (FIG. 7D). As controls, the original mouse anti-**Tac antibody** was also used to stain these cells (FIG. 7B and FIG. 7C), giving similar results...

... Laboratories, Inc., Richmond, Calif.) according to standard techniques. To determine the affinity of the humanized **antibody** relative to the original anti-**Tac antibody** , a competitive binding experiment was performed. About 5X10 sup 5 HUT-102 cells were incubated with known quantities (10-40 ng) of the anti-**Tac antibody** and the humanized anti-**Tac antibody** for 10 min at 4 degree(s) C. Then 100 ng of biotinylated anti-Tac...

...fluorescence on a FACSCAN cytofluorometer.

Use of increasing amounts (10-40 ng) of the anti-**Tac antibody** as competitor in the first step decreased the amount of biotinylated anti-Tac that could...

... if one had greater affinity, it would have more effectively competed with the biotinylated anti-**Tac**, thus decreasing fluorescence more.

Biological properties of the humanized **antibody**
For optimal use in treatment of human disease, the humanized antibody should be able to...

...cell such as a macrophage that can lyse the target. To determine whether the humanized **antibody** and the original mouse anti-**Tac antibody** can mediate ADCC, a chromium release assay was performed by standard methods. Specifically, human **leukemia** HUT-102 cells, which express the IL-2 receptor, were incubated with sup 51 Cr...

... this radionuclide. The HUT-102 cells were then incubated with an excess of either anti-**Tac** or humanized anti-**Tac antibody**. The HUT-102 cells were next incubated for 4 hrs with either a 30:1...is likely to be more efficacious than the original mouse antibody in treating T-cell **leukemia** or other T-cell mediated diseases.

TABLE 3**Antibody**

Anti-**Tac**	4%	<1%	
Humanized anti-**Tac**	24%	23	Higher level expression of the humanized anti-**Tac antibody**

Two new plasmid vectors were prepared for expression of the humanized antibody. The plasmid pVg1...
... Xba I sites of the plasmid vectors pVk and pVG1. To express the humanized anti-**Tac antibody**, the light chain encoding plasmid

was introduced by electroporation into SP2/0 mouse myeloma cells...

... immunoglobulins of the present invention offer numerous advantages of other human IL-2 receptor-specific **antibodies**. In comparison to anti-**Tac** mouse monoclonal **antibodies** , the present human-like immunoglobulin can be more economically produced and contain substantially less foreign... antibody was within about 2-fold of the affinity of the mouse mik- beta 1 **antibody**.

The ability of humanized mik- beta 1 plus humanized anti-**Tac** **antibody** to inhibit IL-2 stimulated proliferation of human lymphocytes was determined. Human mononuclear cells, collected...

... of the antibodies will have strong immunosuppressive properties. Humanized mik- beta 1 plus humanized anti-**Tac** inhibited proliferation much more strongly than did either **antibody** alone.

From the foregoing, it will be appreciated that the humanized immunoglobulins of the present...
... 6. A humanized immunoglobulin according to claim 1, wherein said donor immunoglobulin is the anti-**Tac** **antibody**.

7. A humanized immunoglobulin according to claim 1, wherein said acceptor immunoglobulin heavy and light...

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OTHER REFERENCES

... et al., "Metabolizable sup 111 In Chelate conjugated anti-iodiotype monoclonal antibody for radioimmunodetection of **lymphoma** in mice," J. Nucl. Med. 12:455-460, 1986.

March, Advanced Organic Chemistry, Second edition...

... including monoclonal antibodies specific for tumor-associated antigens in humans. Among the many such monoclonal **antibodies** that may be used are anti-**TAC**, or other interleukin-2 receptor **antibodies**; 9.2.27 and NR-ML-05, reactive with the 250 kilodalton human melanoma-associated...0 degree(s) C. ice bath for 2 minutes.

The Fab fragment of a monoclonal **antibody** (10 **mg** in 0.5 mL of PBS) was generated by **treating** the monoclonal **antibody** with papain according to conventional techniques. The monoclonal **antibody**, designated NR-LU-10, recognizes a pancarcinoma antigen. Other proteins may be substituted for the...

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OTHER REFERENCES

... et al., "Metabolizable sup 111 In chelate conjugated anti-idiotype monoclonal antibody for radioimmunodetection of **lymphoma** in mice", J. Nucl. Med. 12:455-460, 1986.

Meares et al., "Chelate Radiochemistry: cleavable...

...monoclonal anti-bodies specific for tumor-associated antigens in humans. Among the many such monoclonal **antibodies** that may be used are anti-**TAC**, or other interleukin-2 receptor **antibodies**; 9. ...a 0 degree(s) ice bath for 2 minutes.

The Fab fragment of a monoclonal **antibody** (10 **mg** in 0.5 mL of PBS) was generated by **treating** the monoclonal **antibody** with papain according to conventional techniques. The monoclonal **antibody**, designated NR-LU-10, recognizes a pancarcinoma antigen. Other proteins may be substituted for the...

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...81 [1987], 73).

Uchiyama et al (J. Immunol. 126[1981], 1398) described the first monoclonal **antibody** to recognize the **Tac**-antigen (epitope), the short chain of the interleukin-2 receptor.

European Application 0 241 811...

... activated T and B cells but are inactive against quiescent lymphocytes. One of these monoclonal **antibodies**, an anti-**Tac** analogue, enters into interaction with the **Tac**-antigen, the shorter chain of the receptor molecule. The other monoclonal antibody also obviously enters ...

...has not yet been demonstrated.

European Application 0 240 344 concerns anti-CD 4 monoclonal **antibodies** and anti-**Tac** analogues (CD 25). Its activity with respect to immunosuppression and specifically with respect to prevention... monoclonal antibody binds to an epitope of the human interleukin 2 receptor that is not **Tac**. The **antibody** is accordingly appropriate for the treatment of and prophylaxis against such diseases as hyperimmune syndrome...

... encephalomyelitis, arthritis, etc.), and for interleukin-2 receptor expressing tumor diseases such as T-cell **leukemia**.

The monoclonal antibody can be employed either as such, coupled with magnetic beads, radioactive substances...
... PBS) with 10 mu l of test residue or control monoclonal antibody. The control monoclonal **antibodies** in this and in the following examples were the anti-**Tac**-analogous monoclonal **antibodies** BF 2 and BG 8 (CRTS, Besancon). The bound monoclonal antibody was detected with an... cells was tested on days 0 and 4 as in Example 5a. The control monoclonal **antibodies** were the **Tac** analogues
B-F2: CRTS, Besancon (France)
33B3.1: Inserm U 110, Marseille (France)
Clonab IL...risk to infections.

In conjunction with the following clinical-emergency indications, 0.1 to 20 **mg** and preferably 2.5 to 5 **mg** per day of the monoclonal **antibody** B.B.10 were **administered** to the patients within 30 minutes in the form of an intravenous infusion. The dose...

...selected to attain a plasma level of 0.5 to 5 mu g/ml.

The **treatment** was continued for 3 to 30 days and preferably for 7 to 10 days until the interleukin-2-dependent symptoms subsided. **Treatment** beyond that point surprisingly turned out to be unnecessary.

EXAMPLE 8

The amounts of the monoclonal **antibody** B.B.10 (diluted in human albumin) listed in Table 5 were **administered** at the times cited in the table to a group of 4 patients 4, 11...marrow transplantation on the third one. Due to their age, the dosage of the monoclonal **antibody**

B.B.10 was only 2.5 **mg** per day.

Table 6 indicates the doses and duration of **treatment**.

TABLE 6...
? t s3/3/1,21,47,50,54,62,68,70,71

1/3/1
DIALOG(R)File 357:Derwent Biotechnology Abs

0234528 DBA Accession No.: 99-04629 PATENT
Killing cells with immunotoxin - cell lysis using a Pseudomonas sp. exotoxin and single chain antibody scFv fragment fusion, antibody engineering for autoimmune disease and cancer therapy
AUTHOR: Fitzgerald D J; Chaudhary V K; Pastan I H; **Waldmann T A**; Queen C L
CORPORATE SOURCE: Washington, DC, USA.
PATENT ASSIGNEE: U.S.Dep.Health-Hum.Serv. 1999
PATENT NUMBER: US 5863745 PATENT DATE: 990126 WPI ACCESSION NO.: 99-131300 (9911)
PRIORITY APPLIC. NO.: US 461825 APPLIC. DATE: 950605
NATIONAL APPLIC. NO.: US 461825 APPLIC. DATE: 950605
LANGUAGE: English

1/3/2
DIALOG(R)File 357:Derwent Biotechnology Abs

0220988 DBA Accession No.: 98-02585 PATENT
Fusion protein of antibody Fv fragment and Pseudomonas exotoxin fragment - an immunotoxin for use as e.g. an antitumor or immunosuppressive agent
AUTHOR: FitzGerald D; Chaudhary V K; Pastan I H; **Waldmann T A**; Queen C L
CORPORATE SOURCE: Washington, DC, USA.
PATENT ASSIGNEE: U.S.Dep.Health-Hum.Serv. 1997
PATENT NUMBER: US 5696237 PATENT DATE: 971209 WPI ACCESSION NO.: 98-041352 (9804)
PRIORITY APPLIC. NO.: US 463163 APPLIC. DATE: 950605
NATIONAL APPLIC. NO.: US 463163 APPLIC. DATE: 950605
LANGUAGE: English

1/3/3
DIALOG(R)File 357:Derwent Biotechnology Abs

0164255 DBA Accession No.: 94-06806
Genetically engineered monoclonal antibodies armed with radionuclides - radionuclide-carrying anti-Tac monoclonal antibody with reduced immunogenicity (humanized antibody engineering) for interleukin-2 receptor-directed therapy (conference paper)
AUTHOR: **Waldmann T A**
CORPORATE AFFILIATE: Nat.Cancer-Inst.Bethesda Nat.Inst.Health-Bethesda
CORPORATE SOURCE: Metabolism Branch, Bldg 10, Rm 4N115, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.
JOURNAL: BIOTECH'92 (7, 205-12) 1993
CODEN: 9999Q
LANGUAGE: English

1/3/4
DIALOG(R)File 357:Derwent Biotechnology Abs

0123619 DBA Accession No.: 91-11261
Monoclonal antibodies in diagnosis and therapy - monoclonal antibody production; a review
AUTHOR: **Waldmann T A**
CORPORATE SOURCE: Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.
JOURNAL: Science (252, 5013, 1657-62) 1991
CODEN: SCIEAS
LANGUAGE: English

1/3/5
DIALOG(R)File 357:Derwent Biotechnology Abs

0110818 DBA Accession No.: 90-13509
IL2-PE664Glu, a new chimeric protein cytotoxic to human-activated T-lymphocytes - human interleukin-2 gene fusion with Pseudomonas exotoxin mutant gene; potential use of chimeric toxin as cytostatic and immunosuppressive
AUTHOR: Loberboum-Galski H; Garsia R J; Gately M; Brown P S; Clark R E; **Waldmann T A**
CORPORATE AFFILIATE: Roche
CORPORATE SOURCE: Laboratory of Molecular Biology, Division of Cancer Biology and Diagnosis, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
JOURNAL: J.Biol.Chem. (265, 27, 16311-17) 1990
CODEN: JBCHA3
LANGUAGE: English

1/3/6
DIALOG(R)File 357:Derwent Biotechnology Abs

0090949 DBA Accession No.: 89-08940
A recombinant immunotoxin consisting of two antibody variable domains fused to Pseudomonas exotoxin - monoclonal antibody anti-Tac to the p55 subunit of human interleukin-2 receptor
AUTHOR: Chaudhary V K; Queen C; Junghans R P; **Waldmann T A**; FitzGerald D J; Pastan I
CORPORATE AFFILIATE: Protein-Design-Labs
CORPORATE SOURCE: Laboratory of Molecular Biology, DCBD, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
JOURNAL: Nature (339, 6223, 394-97) 1989
CODEN: NATUAS
LANGUAGE: English

1/3/7
DIALOG(R)File 357:Derwent Biotechnology Abs

0054663 DBA Accession No.: 86-12511
Radionuclide-conjugated monoclonal antibodies: a synthesis of immunology, inorganic chemistry and nuclear science - development and application in tumor diagnosis etc.
AUTHOR: Kozak R W; **Waldmann T A**; Atcher R W; Gansow O A
CORPORATE SOURCE: Metabolism Branch, National Cancer Institute of NIH, Bethesda, MD 20892, USA.
JOURNAL: Trends Biotechnol. (4, 10, 259-64) 1986
CODEN: 8921M
LANGUAGE: English

1/3/8
DIALOG(R)File 357:Derwent Biotechnology Abs

0049478 DBA Accession No.: 86-07326
The structure, function, and expression of interleukin-2 receptors on normal and malignant lymphocytes - investigated using a monoclonal antibody
AUTHOR: **Waldmann T A**
CORPORATE SOURCE: Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.
JOURNAL: Science (232, 4751, 727-32) 1986
CODEN: SCIEAS
LANGUAGE: English

1/3/9
DIALOG(R)File 357:Derwent Biotechnology Abs

0005909 DBA Accession No.: 82-04909
A monoclonal antibody that appears to recognize the receptor for human T-cell growth factor; partial characterization of the receptor - purification of the interleukin-2 surface receptor by immunoprecipitation
AUTHOR: Leonard W J; Depper J M; Uchiyama T; Smith K A; **Waldmann T A**; Greene W C
CORPORATE SOURCE: The Metabolism Branch, National Cancer Institute, NIH, Bethesda, Maryland 20205, USA.
JOURNAL: Nature (300, 5889, 267-69) 1982
CODEN: NATUAS
LANGUAGE: English

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  File 399:CA SEARCH(R)  1967-2000/UD=13210
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 3/3/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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12285286   BIOSIS NO.: 200000043153
Patients with chemotherapy-refractory hairy cell leukemia achieve major
  responses to recombinant immunotoxins containing truncated pseudomonas
  exotoxin and targeting either CD25 or CD22.
AUTHOR: Kreitman Robert J(a); Wilson Wyndham H; Margulies Inger(a);
  Stetler-Stevenson Maryalice; Raggio Miranda; FitzGerald David J(a);
  Waldmann Thomas A; Pastan Ira(a
AUTHOR ADDRESS: (a)Laboratory of Molecular Biology, National Cancer
  Institute, NIH, Bethesda, MD**USA
JOURNAL: Blood  94 (10 SUPPL. 1 PART 1):p96a Nov. 15, 1999
CONFERENCE/MEETING: Forty-first Annual Meeting of the American Society of
Hematology  New Orleans, Louisiana, USA  December 3-7, 1999
SPONSOR: The American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Citation
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LANGUAGE: English

3/3/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12266169 BIOSIS NO.: 200000019671
Responses in refractory hairy cell leukemia to a recombinant immunotoxin.
AUTHOR: Kreitman Robert J; Wilson Wyndham H; Robbins David; Margulies Inger ; Stetler-Stevenson Maryalice; **Waldmann Thomas A**; Pastan Ira(a
AUTHOR ADDRESS: (a)National Cancer Institute, National Institutes of Health, 37 Convent Dr, 37/4E16, MSC 4255, Bethesda, MD, 20892**USA
JOURNAL: Blood 94 (10):p3340-3348 Nov. 15, 1999
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

3/3/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12122210 BIOSIS NO.: 199900417059
Methods to avoid adverse effect of circulating antigen on biodistribution of 125I-labeled antiTac dsFv: Preinjection of intact antibody versus clearance of antigen with avidin-biotin system.
AUTHOR: Kobayashi Hisataka; Sun Bao-Fu; Yoo Tae M; Le Nhat; Kim Meyoung-Kon ; Paik Chang H; Pastan Ira; **Waldmann Thomas A**; Carrasquillo Jorge A (a
AUTHOR ADDRESS: (a)Nuclear Medicine Department, National Institutes of Health, 10 Center Dr., Building 10, Rm. 1C-496, Bethesda, MD, 20892-1180 **USA
JOURNAL: Journal of Nuclear Medicine 40 (8):p1381-1391 Aug., 1999
ISSN: 0161-5505
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

3/3/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11990442 BIOSIS NO.: 199900270961
Favorable effects of glycolate conjugation on the biodistribution of humanized antiTac Fab fragment.
AUTHOR: Kobayashi Hisataka; Kim In-sook; Drumm Debbie; Kim Meyoung-kon; Paik David S; Le Nhat; **Waldmann Thomas A**; Carrasquillo Jorge A(a); Paik Chang H
AUTHOR ADDRESS: (a)Department of Nuclear Medicine, National Institutes of Health, 10 Center Dr., MSC 1180, Bldg. 10**USA
JOURNAL: Journal of Nuclear Medicine 40 (5):p837-845 May, 1999
ISSN: 0161-5505
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

3/3/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11848859 BIOSIS NO.: 199900094968
The pharmacokinetic characteristics of glycolated humanized anti-**Tac** Fabs are determined by their isoelectric points.
AUTHOR: Kobayashi Hisataka; Le Nhat; Kim In-Sook; Kim Meyoung-Kon; Pie Jae-Eun; Drumm Debra; Paik David S; **Waldmann Thomas A**; Paik Chang H ; Carrasquillo Jorge A(a
AUTHOR ADDRESS: (a)NIH, Building 10, Room IC496, 10 Center Dr., MSC 1180, Bethesda, MD 20892-1180**USA
JOURNAL: Cancer Research 59 (2):p422-430 Jan. 15, 1999
ISSN: 0008-5472
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11815653 BIOSIS NO.: 199900061762
Reduction in HTLV-I proviral load and spontaneous lymphoproliferation in HTLV-I-associated myelopathy/tropical spastic paraparesis patients treated with humanized anti-**Tac**.
AUTHOR: Lehky Tanya J(a); Levin Michael C; Kubota Ryuji; Bamford Richard N; Flerlage Alfred N; Soldan Samantha S; Leist Thomas P; Xavier Andrew; White Jeffrey D; Brown Margaret; Fleisher Thomas A; Top Lois E; Light Susan; McFarland Henry F; **Waldmann Thomas A**; Jacobson Steven
AUTHOR ADDRESS: (a)HIV Res., DAIDS, NIAID, NIH, 6003 Executive Blvd., Rockville, MD 20892**USA
JOURNAL: Annals of Neurology 44 (6):p942-947 Dec., 1998
ISSN: 0364-5134
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10946921 BIOSIS NO.: 199799568066
Improved biodistribution of 125I-labeled anti-**Tac** disulfide-stabilized Fv fragment by blocking its binding to the alpha subunit of the interleukin 2 receptor in the circulation with preinjected humanized anti-**Tac** IgG.
AUTHOR: Kobayashi Hisataka; Yoo Tae M; Drumm Debra; Kim Meyoung-Kon; Sun Bao-Fu; Le Nhat; Webber Keith O; Pastan Ira; **Waldmann Thomas A**; Paik Chang H; Carrasquillo Jorge A(a
AUTHOR ADDRESS: (a)Nuclear Med. Dep., Build. 10, Room 1C496, NIH, 10 Center Drive, Bethesda, MD 20892-1180**USA
JOURNAL: Cancer Research 57 (10):p1955-1961 1997
ISSN: 0008-5472
RECORD TYPE: Abstract
LANGUAGE: English

3/3/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10154496 BIOSIS NO.: 199698609414
Radioimmunotherapy of interleukin-2R-alpha-expressing adult T-cell leukemia with Yttrium-90-labeled anti-**tac**.
AUTHOR: **Waldmann Thomas A**(a); White Jeffrey D; Carrasquillo Jorge A; Reynolds James C; Paik Chang H; Gansow Otto A; Brechbiel Martin W; Jaffe

Elaine S; Fleisher Thomas A; Goldman Carolyn K; Top Lois E; Bamford Richard; Zaknoen Sara; Roessler Eric; Kasten-Sportes Claude; England Richard; Litou Hariklia; Johnson John A; Jackson-White Terri; Manns Angela; Hanchard Barrie; Junghans Richard P; Nelson David L
AUTHOR ADDRESS: (a)Metabolism Branch, Natl. Cancer Inst. Health, Build. 10, Room 4N115, Bethesda, MD 20892**USA
JOURNAL: Blood 86 (11):p4063-4075 1995
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10119190 BIOSIS NO.: 199698574108
The treatment of HAM/TSP patients with humanized anti-**Tac** antibody: Preliminary immunologic studies.
AUTHOR: Lehky Tanya J; Levin Michael; Flerlage Nick; White Jeffrey; Fleisher Thomas; McFarland Henry; **Waldmann Thomas**; Jacobson Steven
AUTHOR ADDRESS: NIH, Bethesda, MD**USA
JOURNAL: Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology 10 (2):p285 1995
CONFERENCE/MEETING: Seventh International Conference on Human Retrovirology HTLV and Related Viruses Paris, France October 17-21, 1995
ISSN: 1077-9450
RECORD TYPE: Citation
LANGUAGE: English

3/3/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09775306 BIOSIS NO.: 199598230224
Phenotypic knockout of the high-affinity human interleukin 2 receptor by intracellular single-chain antibodies against the alpha subunit of the receptor.
AUTHOR: Richardson Jennifer H; Sodroski Joseph G; **Waldmann Thomas A**; Marasco Wayne A(a
AUTHOR ADDRESS: (a)Dep. Med. Human Retrovirol., Dana-Farber Cancer Inst., Harvard Med. Sch., Boston, MA 02115**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 92 (8):p3137-3141 1995
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/11 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09555739 BIOSIS NO.: 199598010657
Humanized Antibody Directed to the IL-2 Receptor beta-Chain Prolongs Primate Cardiac Allograft Survival.
AUTHOR: Tinubu Sikiru A; Hakimi John; Kondas Jo A; Bailon Pascal; Familletti Philip C; Spence Cheryl; Crittenden Michael D; Parenteau Gary L; Dirbas Fredrick M; Tsudo Mitsuro; Bacher John D; Kasten-Sportes Claude ; Martinucci Jean L; Goldman Carolyn K; Clark Richard E; **Waldmann Thomas A**
AUTHOR ADDRESS: Inq.**USA
JOURNAL: Journal of Immunology 153 (9):p4330-4338 1994

ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/12 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09454744 BIOSIS NO.: 199497463114
Treatment of acute graft-versus-host disease with humanized anti-gac: An antibody that binds to the interleukin-2 receptor.
AUTHOR: Anasetti Claudio(a); Hansen John A; **Waldmann Thomas A**; Appelbaum Frederick R; Davis Jennifer; Deeg H Joachim; Doney Kristine; Martin Paul J; Nash Richard; et al
AUTHOR ADDRESS: (a)Fred Hutchinson Cancer Res. Cent., 1124 Columbia St., E611, Seattle, WA 98104**USA
JOURNAL: Blood 84 (4):p1320-1327 1994
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/13 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09443625 BIOSIS NO.: 199497451995
Radioimmunotherapy of nude mice bearing a human interleukin 2 receptor alpha-expressing lymphoma utilizing the alpha-emitting radionuclide-conjugated monoclonal antibody 212Bi-anti-**Tac**.
AUTHOR: Hartmann Frank; Horak Eva M; Garmestani Kayhan; Wu Chuanchu; Brechbiel Martin W; Kozak Robert W; Tso J; Kosteiny Sheri A; Gansow Otto A; Nelson David L; **Waldmann Thomas A**(a
AUTHOR ADDRESS: (a)Metabolic Branch, Natl. Cancer Inst., Build. 10, 4N115, NIH, Bethesda, MD 20892**USA
JOURNAL: Cancer Research 54 (16):p4362-4370 1994
ISSN: 0008-5472
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/14 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09261813 BIOSIS NO.: 199497270183
Cooperative interactions between the interleukin 2 receptor alpha and beta chains alter the interleukin 2-binding affinity of the receptor subunits.
AUTHOR: Roessler Erich(a); Grant Angus(a); Ju Grace; Tsudo Mitsuru; Sugamura Kazuo; **Waldmann Thomas A**(a
AUTHOR ADDRESS: (a)Metabolism Branch, Natl. Cancer Inst., Natl. Inst. Health, Bethesda, MD 20892**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 91 (8):p3344-3347 1994
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/15 (Item 15 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09039688 BIOSIS NO.: 199497048058
1992 Stohlman Memorial Lecture: Targeting the IL-2 receptor.
AUTHOR: **Waldmann Thomas A**
AUTHOR ADDRESS: Metabolism Branch, Natl. Cancer Inst., Natl. Inst. Health, Bethesda, MD 20892**USA
JOURNAL: Leukemia (Basingstoke) 7 (SUPPL. 2):pS151-S156 1993
ISSN: 0887-6924
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/16 (Item 16 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08974421 BIOSIS NO.: 199396125922
The interleukin-2 receptor: A target for monoclonal antibody treatment of human T-cell lymphotropic virus I-induced adult T-cell leukemia.
AUTHOR: **Waldmann Thomas A**(a); White Jeffrey D; Goldman Carolyn K; Top Lois; Grant Angus; Bamford Richard; Roessler Eric; Horak Ivan D; Zaknoen Sara; et al
AUTHOR ADDRESS: (a)Metabolism Branch, Natl. Cancer Inst., Build. 4N115, Bethesda, MD 20892**USA
JOURNAL: Blood 82 (6):p1701-1712 1993
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/17 (Item 17 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08890746 BIOSIS NO.: 199396042247
Cytotoxic activities of recombinant immunotoxins composed of Pseudomonas toxin or diphtheria toxin toward lymphocytes from patients with adult T-cell leukemia.
AUTHOR: Kreitman Robert J; Chaudhary Vijay K; **Waldmann Thomas A**; Hanchard Barrie; Cranston Beverly; Fitzgerald David J P; Pastan Ira(a
AUTHOR ADDRESS: (a)Lab. Mol. Biol., Div. Cancer Biol., Diagnosis Cent., NCH NIH, 9000 Rockville Pike, 37/4E16, Beth
JOURNAL: Leukemia (Basingstoke) 7 (4):p553-562 1993
ISSN: 0887-6924
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/18 (Item 18 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08785022 BIOSIS NO.: 199395074373
Prolongation of graft survival in primate allograft transplantation by yttrium-90-labeled anti-**Tac** in conjunction with granulocyte colony-stimulating factor.
AUTHOR: Parenteau Gary L; Dirbas Frederick M; Garmestani Kayhan; Brechbiel Martin W; Bukowski Maria A; Goldman Carolyn K; Clark Richard; Gansow Otto A; **Waldmann Thomas A**(a
AUTHOR ADDRESS: (a)Metabolism Branch, National Cancer Inst., Bldg. 10, Room 4N115, National Inst. Health, Bethesda,
JOURNAL: Transplantation (Baltimore) 54 (6):p963-968 1992

ISSN: 0041-1337
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/19 (Item 19 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08751679 BIOSIS NO.: 199395041030
Recombinant toxins containing the variable domains of the anti-**Tac** monoclonal antibody to the interleukin-2 receptor kill malignant cells from patients with chronic lymphocytic leukemia.
AUTHOR: Kreitman Robert J; Chaudhary Vijay K; Kozak Robert W; Fitzgerald David J P; **Waldmann Thomas A**; Pastan Ira(a
AUTHOR ADDRESS: (a)Lab. Mol. Biol., Div. Cancer Biol., Diagnosis and Centers, Natl. Cancer Inst., Natl. Inst. Healt
JOURNAL: Blood 80 (9):p2344-2352 1992
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/20 (Item 20 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08749929 BIOSIS NO.: 199395039280
Mik-beta-1(Fv)-PE40, a recombinant immunotoxin cytotoxic toward cells bearing the beta-chain of the IL-2 receptor.
AUTHOR: Kreitman Robert J; Schneider William P; Queen Cary; Tsudo Mitsuru; Fitzgerald David J P; **Waldmann Thomas A**; Pastan Ira(a
AUTHOR ADDRESS: (a)Lab. Mol. Biol./Div. Cancer Biol., Diagnosis and Centers, 37/4E16, Natl. Cancer Inst., Natl. Ins
JOURNAL: Journal of Immunology 149 (8):p2810-2815 1992
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

potential applications in organ transplantation and the **treatment** of IL-2 receptor-expressing neoplastic diseases.

2/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07421848 BIOSIS NO.: 000091027837
USE OF YTTRIUM-90-LABELED ANTI-TAC ANTIBODY IN PRIMATE XENOGRAFT TRANSPLANTATION
AUTHOR: COOPER M M; ROBBINS R C; GOLDMAN C K; MIRZADEH S; BRECHBIEL M W; STONE C D; GANSOW O A; CLARK R E; WALDMANN T A
AUTHOR ADDRESS: DEP. OF SURG., COLUMBIA UNIV. COLL. OF PHYSICIANS AND SURGEONS, 630 WEST 168TH ST., NEW YORK, N.Y. 10032.
JOURNAL: TRANSPLANTATION (BALTIMORE) 50 (5). 1990. 760-765.
FULL JOURNAL NAME: TRANSPLANTATION (Baltimore)
CODEN: TRPLA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The high-affinity interleukin-2 receptor (IL-2R) is expressed by T cell activated in response to foreign histocompatibility antigens but not by normal resting cells. Thus, blockade of the interaction of IL-2 with its receptor could achieve selective immunosuppression. Accordingly, anti-**Tac**, a murine IgG2a class monoclonal antibody specific to the IL-2R, was used alone or in a chelated form with yttrium-90 (**90Y**), a pure beta emitter, to inhibit rejection of cardiac xenografts from Macaca fascicularis (cynomolgus) donors transplanted to the cervical or abdominal region of Macaca mulatta (rhesus) recipients (n = 20). Animals received no immunosuppression (n = 3, group I, controls), unmodified anti-**Tac** (n = 5, 2 mg/kg q.o.d., group II), or **90Y**-anti-**Tac** (n = 5, 16 mCi, group III). To distinguish the nonspecific immunosuppressive effect of radiation, **90Y** was administered bound to UPC-10 (n = 4, 16 mCi, group IV), another murine monoclonal antibody that does not specifically recognize activated immunoresponsive cells. All immunosuppression was administered in divided doses during the first 2 weeks posttransplant. Group I animals rejected their grafts at 6.7 .+-. 1 days and demonstrated a rise is soluble IL-2R levels at the time of rejection, indicating the generation of **Tac**-expressing and -releasing cells. Graft survival in group II was not prolonged compared with controls (mean survival 6.2 .+-. 1 days; P > 0.05). In contrast, graft survival in animals that received the designed dosage of **90Y**-anti-**Tac** was significantly prolonged to an average of 38.4 .+-. 5 days compared with groups I and II (P < 0.005 and P < 0.0005, respectively). Prolongation of graft survival occurred in animals that received **90Y**-UPC-10 (mean survival 21.3 .+-. 5 days, P < 0.05 versus group I, P < 0.01 versus group II). However, **90Y**-UPC-10 was significantly less effective in prolonging graft survival than **90Y**-anti-**Tac**, in which one-half the per-kilogram dosage of radioactivity was delivered in specific fashion via anti-**Tac** (P < 0.025). Reversible nonlethal bone marrow suppression occurred without associated nephro- or hepatotoxicity, and virtually all animals developed antibodies to the urine monoclonal. Thus, the approach used in the present study, IL-2R-directed therapy with **90Y**-anti-**Tac**, may have potential applications in organ transplantation and in the treatment of **Tac**-expressing neoplastic diseases.

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E12       5  AU=WALDRAFF W

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 1/3/1
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0234528  DBA Accession No.: 99-04629    PATENT
Killing cells with immunotoxin - cell lysis using a Pseudomonas sp.
    exotoxin and single chain antibody scFv fragment fusion, antibody
    engineering for autoimmune disease and cancer therapy
AUTHOR: Fitzgerald D J;  Chaudhary V K;  Pastan I H;  Waldmann T A;
    Queen C L
CORPORATE SOURCE: Washington, DC, USA.
PATENT ASSIGNEE: U.S.Dep.Health-Hum.Serv.  1999
PATENT NUMBER: US 5863745  PATENT DATE: 990126  WPI ACCESSION NO.:
    99-131300  (9911)
PRIORITY APPLIC. NO.: US 461825  APPLIC. DATE: 950605
NATIONAL APPLIC. NO.: US 461825  APPLIC. DATE: 950605
LANGUAGE: English


 1/3/2
DIALOG(R)File 357:Derwent Biotechnology Abs
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0220988  DBA Accession No.: 98-02585    PATENT
Fusion protein of antibody Fv fragment and Pseudomonas exotoxin fragment -
    an immunotoxin for use as e.g. an antitumor or immunosuppressive agent
AUTHOR: FitzGerald D;  Chaudhary V K;  Pastan I H;  Waldmann T A;
    Queen C L
CORPORATE SOURCE: Washington, DC, USA.
PATENT ASSIGNEE: U.S.Dep.Health-Hum.Serv.  1997
PATENT NUMBER: US 5696237  PATENT DATE: 971209  WPI ACCESSION NO.:
    98-041352  (9804)
PRIORITY APPLIC. NO.: US 463163  APPLIC. DATE: 950605
NATIONAL APPLIC. NO.: US 463163  APPLIC. DATE: 950605
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LANGUAGE: English

1/3/3
DIALOG(R)File 357:Derwent Biotechnology Abs
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0164255 DBA Accession No.: 94-06806
Genetically engineered monoclonal antibodies armed with radionuclides - radionuclide-carrying anti-Tac monoclonal antibody with reduced immunogenicity (humanized antibody engineering) for interleukin-2 receptor-directed therapy (conference paper)
AUTHOR: **Waldmann T A**
CORPORATE AFFILIATE: Nat.Cancer-Inst.Bethesda Nat.Inst.Health-Bethesda
CORPORATE SOURCE: Metabolism Branch, Bldg 10, Rm 4N115, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.
JOURNAL: BIOTECH'92 (7, 205-12) 1993
CODEN: 9999Q
LANGUAGE: English

1/3/4
DIALOG(R)File 357:Derwent Biotechnology Abs
(c) 2000 Derwent Publ Ltd. All rts. reserv.

0123619 DBA Accession No.: 91-11261
Monoclonal antibodies in diagnosis and therapy - monoclonal antibody production; a review
AUTHOR: **Waldmann T A**
CORPORATE SOURCE: Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.
JOURNAL: Science (252, 5013, 1657-62) 1991
CODEN: SCIEAS
LANGUAGE: English

1/3/5
DIALOG(R)File 357:Derwent Biotechnology Abs
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0110818 DBA Accession No.: 90-13509
IL2-PE664Glu, a new chimeric protein cytotoxic to human-activated T-lymphocytes - human interleukin-2 gene fusion with Pseudomonas exotoxin mutant gene; potential use of chimeric toxin as cytostatic and immunosuppressive
AUTHOR: Loberboum-Galski H; Garsia R J; Gately M; Brown P S; Clark R E; **Waldmann T A**
CORPORATE AFFILIATE: Roche
CORPORATE SOURCE: Laboratory of Molecular Biology, Division of Cancer Biology and Diagnosis, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
JOURNAL: J.Biol.Chem. (265, 27, 16311-17) 1990
CODEN: JBCHA3
LANGUAGE: English

1/3/6
DIALOG(R)File 357:Derwent Biotechnology Abs
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0090949 DBA Accession No.: 89-08940
A recombinant immunotoxin consisting of two antibody variable domains fused to Pseudomonas exotoxin - monoclonal antibody anti-Tac to the p55 subunit of human interleukin-2 receptor
AUTHOR: Chaudhary V K; Queen C; Junghans R P; **Waldmann T A**; FitzGerald D J; Pastan I

CORPORATE AFFILIATE: Protein-Design-Labs
CORPORATE SOURCE: Laboratory of Molecular Biology, DCBD, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
JOURNAL: Nature (339, 6223, 394-97) 1989
CODEN: NATUAS
LANGUAGE: English

1/3/7
DIALOG(R)File 357:Derwent Biotechnology Abs

0054663 DBA Accession No.: 86-12511
Radionuclide-conjugated monoclonal antibodies: a synthesis of immunology, inorganic chemistry and nuclear science - development and application in tumor diagnosis etc.
AUTHOR: Kozak R W; **Waldmann T A**; Atcher R W; Gansow O A
CORPORATE SOURCE: Metabolism Branch, National Cancer Institute of NIH, Bethesda, MD 20892, USA.
JOURNAL: Trends Biotechnol. (4, 10, 259-64) 1986
CODEN: 8921M
LANGUAGE: English

1/3/8
DIALOG(R)File 357:Derwent Biotechnology Abs

0049478 DBA Accession No.: 86-07326
The structure, function, and expression of interleukin-2 receptors on normal and malignant lymphocytes - investigated using a monoclonal antibody
AUTHOR: **Waldmann T A**
CORPORATE SOURCE: Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.
JOURNAL: Science (232, 4751, 727-32) 1986
CODEN: SCIEAS
LANGUAGE: English

1/3/9
DIALOG(R)File 357:Derwent Biotechnology Abs

0005909 DBA Accession No.: 82-04909
A monoclonal antibody that appears to recognize the receptor for human T-cell growth factor; partial characterization of the receptor - purification of the interleukin-2 surface receptor by immunoprecipitation
AUTHOR: Leonard W J; Depper J M; Uchiyama T; Smith K A; **Waldmann T A**; Greene W C
CORPORATE SOURCE: The Metabolism Branch, National Cancer Institute, NIH, Bethesda, Maryland 20205, USA.
JOURNAL: Nature (300, 5889, 267-69) 1982
CODEN: NATUAS
LANGUAGE: English

DIALOG(R)File 357:Derwent Biotechnology Abs

0234528 DBA Accession No.: 99-04629 PATENT
Killing cells with immunotoxin - cell lysis using a Pseudomonas sp. exotoxin and single chain antibody scFv fragment fusion, antibody engineering for autoimmune disease and cancer therapy
AUTHOR: Fitzgerald D J; Chaudhary V K; Pastan I H; **Waldmann T A**; Queen C L
CORPORATE SOURCE: Washington, DC, USA.
PATENT ASSIGNEE: U.S.Dep.Health-Hum.Serv. 1999
PATENT NUMBER: US 5863745 PATENT DATE: 990126 WPI ACCESSION NO.: 99-131300 (9911)
PRIORITY APPLIC. NO.: US 461825 APPLIC. DATE: 950605
NATIONAL APPLIC. NO.: US 461825 APPLIC. DATE: 950605
LANGUAGE: English

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AUTHOR: FitzGerald D; Chaudhary V K; Pastan I H; **Waldmann T A**; Queen C L
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PATENT NUMBER: US 5696237 PATENT DATE: 971209 WPI ACCESSION NO.: 98-041352 (9804)
PRIORITY APPLIC. NO.: US 463163 APPLIC. DATE: 950605
NATIONAL APPLIC. NO.: US 463163 APPLIC. DATE: 950605
LANGUAGE: English

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0164255 DBA Accession No.: 94-06806
Genetically engineered monoclonal antibodies armed with radionuclides - radionuclide-carrying anti-Tac monoclonal antibody with reduced immunogenicity (humanized antibody engineering) for interleukin-2 receptor-directed therapy (conference paper)
AUTHOR: **Waldmann T A**
CORPORATE AFFILIATE: Nat.Cancer-Inst.Bethesda Nat.Inst.Health-Bethesda
CORPORATE SOURCE: Metabolism Branch, Bldg 10, Rm 4N115, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.
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CORPORATE SOURCE: Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.
JOURNAL: Science (252, 5013, 1657-62) 1991
CODEN: SCIEAS
LANGUAGE: English

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DIALOG(R)File 357:Derwent Biotechnology Abs

0110818 DBA Accession No.: 90-13509
IL2-PE664Glu, a new chimeric protein cytotoxic to human-activated T-lymphocytes - human interleukin-2 gene fusion with Pseudomonas exotoxin mutant gene; potential use of chimeric toxin as cytostatic and immunosuppressive
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CORPORATE AFFILIATE: Roche
CORPORATE SOURCE: Laboratory of Molecular Biology, Division of Cancer Biology and Diagnosis, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
JOURNAL: J.Biol.Chem. (265, 27, 16311-17) 1990
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AUTHOR: Chaudhary V K; Queen C; Junghans R P; **Waldmann T A**; FitzGerald D J; Pastan I
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CORPORATE SOURCE: Metabolism Branch, National Cancer Institute of NIH, Bethesda, MD 20892, USA.
JOURNAL: Trends Biotechnol. (4, 10, 259-64) 1986
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LANGUAGE: English

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A monoclonal antibody that appears to recognize the receptor for human T-cell growth factor; partial characterization of the receptor - purification of the interleukin-2 surface receptor by immunoprecipitation
AUTHOR: Leonard W J; Depper J M; Uchiyama T; Smith K A; **Waldmann T A**; Greene W C
CORPORATE SOURCE: The Metabolism Branch, National Cancer Institute, NIH, Bethesda, Maryland 20205, USA.
JOURNAL: Nature (300, 5889, 267-69) 1982
CODEN: NATUAS
LANGUAGE: English

7/3/42 (Item 13 from file: 73)
DIALOG(R)File 73:EMBASE

07162127 EMBASE No: 1998050169
Clinical pharmacology and therapeutic potential of monoclonal antibody treatment in rheumatoid **arthritis**
Choy E.H.S.
Dr. E.H.S. Choy, Rheumatology Unit, Thomas Guy House, Guy's Hospital, St Thomas Street, London SE1 9RT United Kingdom
AUTHOR EMAIL: e.choy@umds.ac.uk
Drugs and Aging (DRUGS AGING) (New Zealand) 1998, 12/2 (139-148)
CODEN: DRAGE ISSN: 1170-229X
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

7/3/38 (Item 9 from file: 73)
DIALOG(R)File 73:EMBASE

07247945 EMBASE No: 1998138658
Biological agents in rheumatoid **arthritis**: Which ones could be used in combination?
Lorenz H.-M.; Kalden J.R.
Dr. H.-M. Lorenz, Department of Medicine III, Inst. Clinical Immunol./Rheumatology, University of Erlangen-Nuremberg, Krankenhausstrasse 12, 91054 Erlangen Germany
AUTHOR EMAIL: Hannes.Lorenz@med3.med.uni-erlangen.de
BioDrugs (BIODRUGS) (New Zealand) 1998, 9/4 (303-324)
CODEN: BIDRF ISSN: 1173-8804
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 130

7/3/32 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

07932003 EMBASE No: 1999405331
Novel biologic approaches to the treatment of rheumatoid **arthritis**
Sany J.
Prof. J. Sany, Service d'Immuno-Rhumatologie, Hopital Lapeyronie, 34295 Montpellier Cedex 2 France
Revue du Rhumatisme (English Edition) (REV. RHUM. ENGL. ED.) (France) 1999, 66/11 (548-559)
CODEN: RRHUE ISSN: 1169-8446
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 73

7/3/33 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

07768530 EMBASE No: 1999247338
What we have learned from trials of immunomodulatory agents in rheumatoid **arthritis**: Future directions
Schulze-Koops H.; Burkhardt H.; Kalden J.R.
Dr. H. Schulze-Koops, Department of Internal Medicine III, University of Erlangen-Nuremberg, Krankenhausstrasse 12, D-91054 Erlangen Germany
Drugs of Today (DRUGS TODAY) (Spain) 1999, 35/4-5 (327-351)
CODEN: MDACA ISSN: 0025-7656
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 172

7/3/28 (Item 28 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07982165 BIOSIS NO.: 000042033563
HUMANIZED MONOCLONAL ANTIBODY TREATMENT IN RHEUMATOID **ARTHRITIS**
AUTHOR: KYLE V; RODDY J; HALE G; HAZLEMAN B L; WALDMANN H
AUTHOR ADDRESS: RHEUMATOLOGY RESEARCH UNIT, ADDENBROOKE'S HOSPITAL, CAMBRIDGE, UK.
JOURNAL: J RHEUMATOL 18 (11). 1991. 1737-1738.
FULL JOURNAL NAME: Journal of Rheumatology
CODEN: JRHUA
RECORD TYPE: Citation
LANGUAGE: ENGLISH

7/3/29 (Item 29 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06744219 BIOSIS NO.: 000088053649
BENEFICIAL EFFECT OF MONOCLONAL ANTIBODY TO INTERLEUKIN 2 RECEPTOR ON ACTIVATED T CELLS IN RHEUMATOID **ARTHRITIS**
AUTHOR: KYLE V; COUGHLAN R J; TIGHE H; WALDMANN H; HAZLEMAN B L
AUTHOR ADDRESS: RHEUMATOL. RES. UNIT., UNIT E6, ADDENBROOKE'S HOSP., HILLS ROAD, CAMBRIDGE CB2 2QQ.
JOURNAL: ANN RHEUM DIS 48 (5). 1989. 428-429.
FULL JOURNAL NAME: Annals of the Rheumatic Diseases
CODEN: ARDIA
RECORD TYPE: Abstract